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ARCHIVES OF SURGERY

VOLUME 22 MAY, 1931 NUMBER 5

INTRAPERITONEAL PRESSURE *

RICHARD H. OVERHOLT, M.D.

PHILADELPHIA

Pressure conditions which exist within the peritoneal cavity have received much less attention than that given to considerations of the pressure within other body cavities. Since one understands pressure to be the action of a force against an opposing force, it is possible to think of a pressure within the cleft between the parietal and the opposing visceral peritoneum.

Under normal conditions the peritoneal cavity, as it is known anatomically, is not a cavity but a cleft. However, in this discussion the term peritoneal cavity will, because of its wider usage, be used to denote the potential peritoneal space, or, more strictly speaking, the peritoneal cleft. The ramifications of this cleft extend, for the most part, throughout the abdominal cavity and between the various organs. Nothing is contained within this space except a small amount of peritoneal fluid which moistens its surfaces. There is no communication with the outside except through the fallopian tubes in the female, and this communication is of no practical importance so far as pressures are concerned. The reflections of the parietal peritoneum conform, for the most part, to the limitations of the abdominal cavity. Since practically all of the remainder of the peritoneum covers the viscera and moves about within the parietal peritoneum, the consideration of pressure values between these components of the peritoneum are, for all practical purposes, considerations of pressure values within the so-called abdominal cavity.

Mechanically, the abdomen has been considered by Krause,[1] Hitzenberger [2] and Wildegras [3] as a closed box with partially rigid and partially flexible walls, so that pressure values would follow hydrostatic laws for such containers. The degree of flexibility of the walls and the specific gravity of the contents would determine the pressure at any given point. With a portion of the container rigid (spine) and an anchorage above

* Submitted for publication, June 13, 1930.

* From the Laboratory of Research Surgery and the Department of Surgery (Division B) University of Pennsylvania, aided by a grant from the Duane Fund.

1. Krause, N. J.: Der intraabdominelle Druck im Bereiche Epigastriums und dessen Bedeutung in der Magenchirurgie, Arch. f. klin. Chir. **144**:201, 1927.

2. Hitzenberger, K.: Zwerchfall und Intraperitoneal Druck, Klin. Wchnschr. **8**:961 (May) 1929.

3. Wildegras, H.: Ueber den intraperitonealen Druck, Mitt. a. d. Grenzgeb. d. Med. u. Chir. **37**:308, 1923.

(costal arch), there is a tendency for the container to maintain its shape in various positions. The weight of the contents causes a bulging in the dependent portions and a sinking in the upper portions (fig. 1).

Simple mechanical explanations of pressure alterations in the abdominal cavity are complicated by a movable partition above (the diaphragm), by attachments to a shifting costal arch, by living contractile abdominal walls and by contained viscera some of which may be full or empty and may contain gas collections, fluid or solid matter.

There has been considerable speculation as to the pressure conditions that exist within the peritoneal cavity. Many investigators have reported work on intra-abdominal pressure by recording volume changes in balloons inserted in the rectum, stomach or bladder. This determined intra-intestinal or intravesicular pressure and not intraperitoneal pressure. According to Keppich,[4] Winkler was the first to measure pressures in the peritoneal cavity by inserting a trocar and connecting it with a water manometer. In a similar way, many other investigators have measured the intraperitoneal pressure. There has been consider-

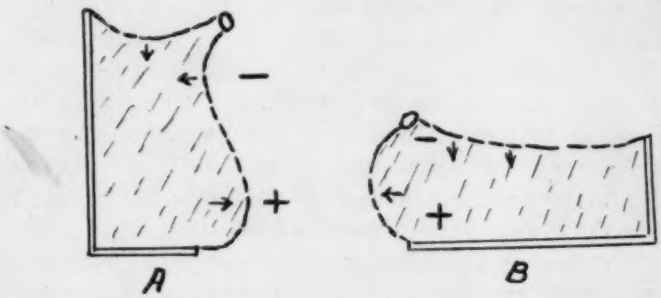

Fig. 1.—Diagram of an airtight container with partially rigid and partially distensible walls filled with fluid. (After Krause.) The effects of gravitation on pressure exerted at various points are shown; *A*, erect position; *B*, horizontal position. The anchorage of the flexible walls above corresponds in the diagram to the part the spine and costal arch play in the upper part of the abdomen.

able disagreement as to whether it is above or below atmospheric pressure. Kelling,[5] Hormann[6] and others thought it necessary to inject air or water before the pressure could be measured. Such injections in themselves alter the existing pressure. Likewise, all observations on patients with ascites at the time of an abdominal paracentesis do not represent the true pressure. Quirin[7] and others first opened the peri-

4. Keppich, J.: Intraperitoneal Druck, Arch. f. klin. Chir. **116**:276, 1921.

5. Kelling, G.: Quoted by Keppich, footnote 4.

6. Hormann, K.: Quoted by Emerson, footnote 8.

7. Quirin, A.: Ueber das Verhalten des normalen und pathologisch gesteigerten intraabdominalen Druckes und seine Rückwirkung auf die arterielle Blutcirculation, Deutsches Arch. f. klin. Med. **71**:79, 1901.

toneal cavity and then sutured a cannula in place. This method is also open to the same objection.

In 1911, Emerson [8] made an exhaustive review of the literature on this subject, and concluded that the majority of investigators had found a pressure in the peritoneal cavity which exceeded atmospheric pressure. During his own experiments on rabbits and dogs, he made similar observations.

More recently, Wildegras [3] has contended that the intraperitoneal pressure is as a rule slightly greater than atmospheric pressure. Keppich,[4] Melchior and Melchior,[9] Wagoner [10] and others have consistently recorded subatmospheric pressures by using a large bore needle cannula and a water manometer.

Practically all investigators have reported shifts in the intraperitoneal pressures with the phases of respiration, as evidenced by an inspiratory increase (diaphragmatic contraction) and an expiratory decrease (diaphragmatic relaxation) in pressure. Keppich [4] was unable to record these variations, and he also pointed out that it was impossible to influence the intraperitoneal pressure by straining, by pressure on the chest or by shifting the position of the animal.

Much of the confusion is undoubtedly due to two things: 1. Most investigators have taken pressure readings at only one point in the abdomen. 2. All have used a needle or cannula connected with a water manometer. Whenever the open U-tube water manometer is used to measure pressures, the shift of the column of water in the manometer produces a corresponding displacement of air in the connecting tube and cannula. If the pressure is below atmospheric pressure, a certain amount of air is lost from the measuring system and passes into the abdomen. If the intraperitoneal pressure exceeds atmospheric pressure, the displacement required to effect a shift of the manometer causes the visceral peritoneum to seal the openings in the cannula, and a true pressure cannot be registered. It is probably because of this difficulty in measuring pressures greater than atmospheric pressure that many investigators record readings only in the epigastrium, where the pressure is usually subatmospheric. Wagoner [10] evidently had the same trouble, for he says: "No intra-abdominal pressure readings are obtainable with the animal in this position (horizontal) if the needle be inserted posteriorly or posterolaterally, due to the posterior gravitation of the abdominal viscera."

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8. Emerson, H.: Intra-abdominal Pressures, Arch. Int. Med. **7**:754, 1911.

9. Melchior, E., and Melchior, P.: Intraperitoneal Druck, Arch. f. klin. Chir. **119**:148, 1922.

10. Wagoner, G. W.: Studies on Intra-abdominal Pressure, Am. J. M. Sc. **171**:697 (May) 1926.

METHOD

Dogs were used in all of these experiments. In most instances, the animals were anesthetized with one of the barbital derivatives, 50 mg. per kilogram of body weight being administered. The barbital derivative was administered intravenously in some and intraperitoneally in others. No differences in the results were observed as a consequence of the method of administering the anesthetic. Observations were also made on trained, unanesthetized dogs, the cannula being inserted after the local infiltration of procaine hydrochloride. Animals were also observed immediately after death.

An adjustable table was used so that the position of the dog could be changed without effecting the recording apparatus. The animal could be fastened to this table and tilted head up or head down or rotated on the horizontal axis so that the anterior abdominal wall was above, on the side or dependent.

A right-angled cannula was devised which could be inserted through a small incision in the skin, and pushed into the peritoneal cavity without the possibility

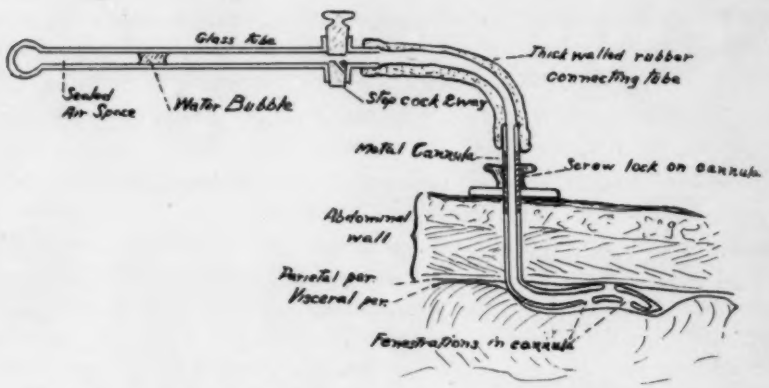

Fig. 2.—Diagram of the apparatus used in measuring intraperitoneal pressure. The variations of pressure within the cannula cause a fluctuation of the water bubble in the closed manometer, which was designed by Lewis. The instrument was calibrated against a water manometer and the linear displacement of the water bubble noted under a microscope or projected on a movable photographic screen. A water bath is constructed about the manometer. This is not shown in the diagram.

of the entrance of air. The cannula was made with a solid tip and several side openings, so that occlusion of the lumen would not take place. A thumb screw and washer were placed on the shaft so that the cannula could be held securely in place without the possibility of shifting or leakage (fig. 2). The cannula was introduced in different locations of the abdomen. For measuring the pressure in the upper portion of the peritoneal cleft, the cannula was inserted in the epigastrium either to the right or the left of the midline. For the pressure in the lower peritoneal cleft, the cannula was inserted in the right or left lower quadrant. In determining the pressure in the posterior portion of the peritoneal cleft, the right or left costovertebral angle was used as the point of entrance for the cannula.

For recording the pressure changes various methods were used. In the first animals studied, a water manometer was connected directly to the cannula before it was inserted. In some, a tambour was connected, and tracings were made on a smoked drum. The objections to the direct measurement of the pressure by the U-tube manometer were overcome by the use of a closed system manometer devised by Lewis.[11] This instrument consists of a hollow glass tube sealed at one end, a water bubble in the shaft of the tube and a two-way stop-cock at the opposite end (fig. 2). With this tube connected to the cannula in the abdomen, variations in pressure cause a shift of the bubble. The movement of the bubble is, however, reduced because of the sealed end of the glass tube, its amplitude for any given pressure being determined by the volume of the air in the sealed space. The exact linear displacement of the bubble was so small that it was necessary to take the measurements with microscopic magnification. The portion of the water bubble at atmospheric pressure was determined by opening the stop-cock and at the same time closing off that part of the system which was in communication with the peritoneal cavity. A water bath constructed about the manometer prevented any changes in volume as a result of temperature variations. Photographic records of the movement of the bubble of water were made by projecting a beam of light through the microscope and focusing it on a moving film. For this the recording part of an electrocardiograph was used. Each closed manometer tube was carefully calibrated against a water manometer and by actual calculation. Such a method met most of the objections of the open system. The volume shift at the end of the cannula was estimated to be less than 3 or 4 mm., so that positive pressures could be measured without the valvelike occlusion of the cannula openings by the visceral peritoneum. Capillarity of the water column in the manometer was avoided. The factor of inertia of the water column in the U-tube manometer was eliminated.

Various procedures were carried out for the purpose of altering the pressure within the peritoneal cavity. Moderate pressure of the hand on the abdomen and the application of a muslin binder were used to alter the flexibility of the anterior abdominal wall. The stomach and colon were distended by inflating balloons after their insertion.

Known amounts of air were injected into the abdomen to study the effects of pneumoperitoneum on the intraperitoneal pressure. One animal was eviscerated, the abdominal cavity filled with water, and the abdominal wall closed. In this animal pressure observations were made with the same apparatus that was used in the living animal.[12]

RESULTS

Animal on Its Back in Horizontal Position.—With the cannula in the epigastrium readings were made on thirty-three animals. A mean subatmospheric pressure was recorded in thirty-two of the animals. This mean is the value between inspiration and expiration. The values

11. Lewis, R. M.: A Closed System Manometer, to be published.

12. At the suggestion of Prof. H. C. Bazett, of the Department of Physiology, one observation was made on the intraperitoneal pressure after the insertion of a cannula in the epigastrium with the dog in the horizontal position. A method of mirror reflexion was used, and subatmospheric pressures were demonstrated.

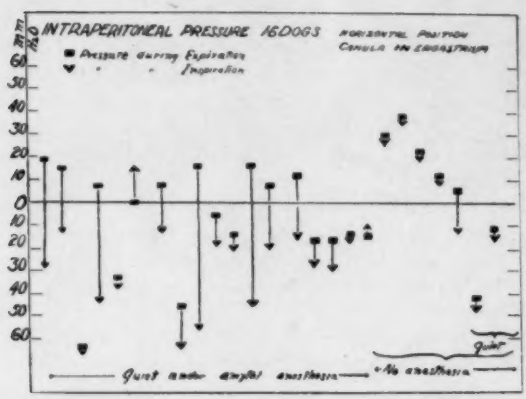

Fig. 3.—Graph showing intraperitoneal pressure values obtained in sixteen animals. The cannula was in the epigastrium and the animals placed on their backs in the horizontal position. The extremes of the arrows show the actual pressure variation during the two phases of respiration. Note that the majority of the readings were below atmospheric pressure, and that the pressure fell during inspiration in all but two instances.

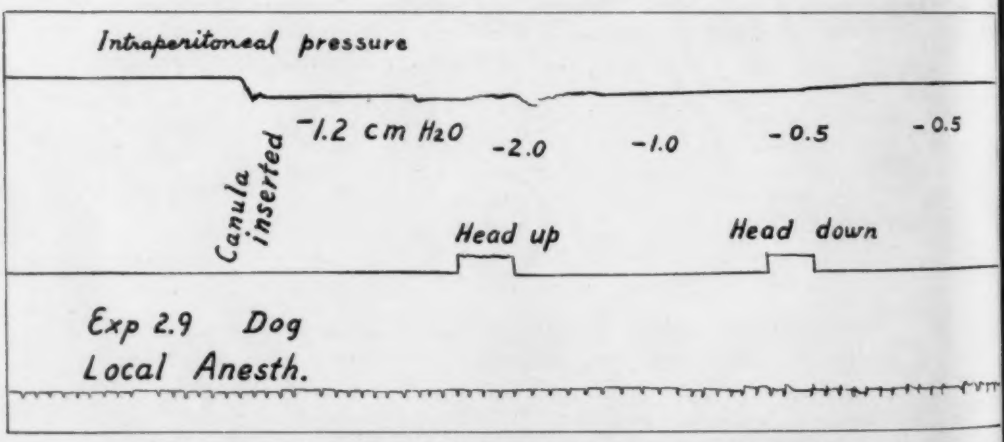

Fig. 4 (dog 203).—Weight of animal, 19 Kg. Kymographic tracing showing curve of the intraperitoneal pressure with animal on its back in a horizontal position. Local anesthesia was used. Note the drop in the pressure from the atmospheric level as cannula was inserted and the absence of marked changes in pressure with alterations of position due to the lack of anesthesia. Note the absence of respiratory excursions in this record. The readings were recorded in centimeters of water pressure.

varied from 5 to 100 mm. of water pressure. In one animal the pressure was zero (fig. 3). Subatmospheric pressures were also obtained in two dead animals. In three animals in which no anesthesia was given, the intraperitoneal pressure in the epigastrium was below the atmospheric value in two and above in one (fig. 4).

No relationship could be worked out between the weight of the animals and the pressure found in the peritoneal cavities of the animals in the horizontal position. Pressures were found to be lowest when the animal was deeply anesthetized. Under such conditions, the pressure became even still lower if the legs of the animal were stretched so that the concavity of the anterior abdominal wall approached a straight line. If the animal was lightly anesthetized or was straining, the pressure became greater, and its rise was even more marked when the legs were stretched; that is, the pressure values were reversed.

Relation of Respiration to Intraperitoneal Pressure.—In the experiments in which the U-tube manometer was used, we were unable normally to detect fluctuations in the intraperitoneal pressures caused by the respiratory excursions. Following the injection of a small amount (from 2 to 5 cc.) of air into the peritoneal cavity at the site of the cannula, respiratory excursions could be recorded.

However, we were able to observe in the normal animal variations in pressure with the respiratory phases without the induction of a pneumoperitoneum by using the closed water bubble manometer devised by Lewis (figs. 5, 6 and 7). In seventeen animals that were breathing quietly and regularly it was found that the pressure in the peritoneal cavity decreased during inspiration and increased during expiration. This is contrary to the results obtained by other observers.

The same inspiratory decrease in the intraperitoneal pressure was noted when the cannula was inserted in the lower part of the abdomen, or in the costovertebral angle. The same observation was made in the animals that had only local anesthesia for the insertion of the needles. In fact, a change in the position of the animals did not alter this relation of pressure variation to the respiratory phase so long as the quiet, even type of breathing was undisturbed.

However, if the animal strained under light anesthesia, struggled under no anesthesia, or had an irregular abdominal type of breathing, the pressure variations within the peritoneal cavity were reversed, i. e., the increase was noted during inspiration (diaphragmatic descent) and was decreased during expiration (diaphragmatic relaxation).

Relative Positions of the Cannula and the Animal.—With the cannula in the lower part of the abdomen and the animal placed in the horizontal position, the mean pressure in the majority of instances was

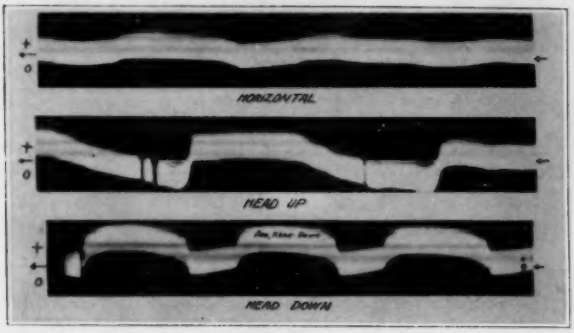

Fig. 5 (dog 615).—Photograph on a moving screen of meniscus of the water bubble in a closed manometer. The cannula was in the epigastrium. The dogs were anesthetized with a barbital derivative. The white line through the center was set at atmospheric pressure. Note the variations from this line with the change in position. Also note that the pressure during the short inspiratory phase is decreased. The animal was on its back. (Experiment 62, weight of animal, 12 Kg.)

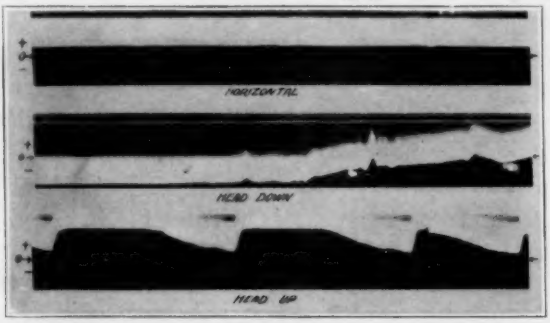

Fig. 6 (dog 615).—Photograph showing pressure changes in the lower part of the abdomen with shifts in position. Note that in the horizontal position the pressure is above the atmospheric level, as indicated by the white line. The pressure decreases with the inspiratory phase. Note that the pressure shifts are the reverse of those obtained with the cannula in the epigastrium (fig. 5). The animal was on its back. (Experiment 62.)

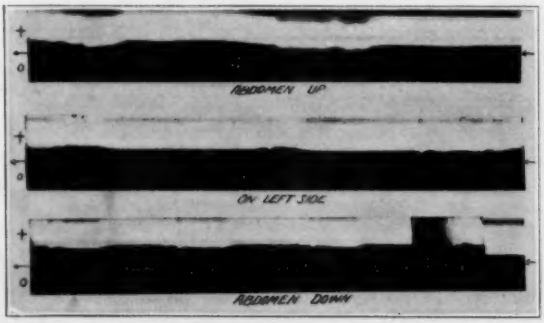

Fig. 7 (dog 615).—Photograph showing pressure changes as registered in the Lewis manometer with rotation of the animal in the horizontal position. As the animal is turned so that the abdomen is dependent, the pressure increases. The cannula was in the lower part of the abdomen. (Experiment 62.)

above atmospheric pressure (fig. 6). However, in many of the animals the pressure fell to a subatmospheric level at the height of inspiration (table 1).

With the animal on its back, a shift to the vertical head-up position caused a marked fall in the intraperitoneal pressure in the upper part of the abdomen and an increase of the pressure in the lower part of the abdomen. These results were reversed when the animals were put in a vertical head-down position.

In an animal weighing 9 Kg., which was eviscerated and the abdomen filled with water, a similar shift in pressure followed alterations in position. In the horizontal position a zero pressure was recorded in the

Intraperitoneal Pressure Variations with Relation to the Relative Positions of the Cannula and the Animal in Three Experiments, Expressed in Millimeters of Water

		Experiment 49 Dog 476, Wt. 8 Kg.		Experiment 54 Dog 536, Wt. 9 Kg.		Experiment 52 Dog 203, Wt. 19 Kg.	
Position of Cannula	Position of Animal (on Back)	Mm. Inspiration	Mm. Expiration	Mm. Inspiration	Mm. Expiration	Mm. Inspiration	Mm. Expiration
Epigastrium	Horizontal	— 47	+ 16	— 26	— 20	— 35	— 32
Epigastrium	Head up	— 58	+ 89	— 155	+ 50	— 67	— 69
Epigastrium	Head down	+ 49	+ 87	— 10	+ 73	+ 7.5	+ 53
Lower part of abdomen	Horizontal	— 25	+ 8	.....	+ 20	— 30	+ 12
Lower part of abdomen	Head up	+ 103	+ 1	+ 34	+ 130	+ 125	+ 137
Lower part of abdomen	Head down	— 127	— 100	— 46	— 38	— 37.6	+ 15

epigastrium. In the head-down position, the pressure was + 108 mm. and in the head-up position — 32 mm. of water.

When the normal anesthetized animal was shifted to a lateral position with the cannula anywhere in the central portion of the anterior abdominal wall, the intraperitoneal pressure increased. The rise in the intraperitoneal pressure was even more marked when the animal was turned completely over so that the abdomen was down.

With the cannula in the left costovertebral angle and the animal on its back, a positive intraperitoneal pressure was recorded. The pressure decreased to a subatmospheric value if the animal was turned so that the abdomen was hanging dependent.

The Effect of Abdominal Manipulations on the Intraperitoneal Pressure.—Procedures that restricted the movement of the anterior abdominal wall, such as pressure of the hand on the abdomen, the application of an abdominal binder or the inflation of the stomach or colon tended slightly to increase the intraperitoneal pressure. However, the increase in pressure was barely sufficient to raise it above the atmospheric level when measured in the epigastrium (fig. 8).

Pneumoperitoneum.—Following the injection of 100 cc. of air, an immediate shift from subatmospheric pressure values to values above atmospheric pressure occurred. Subsequent injections of air caused a slight, but not proportional, increase in the intraperitoneal pressure

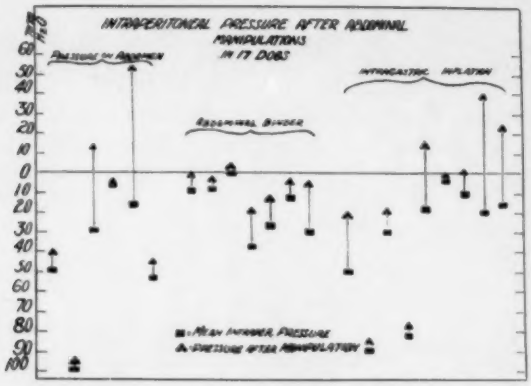

Fig. 8.—Chart showing effects of pressure on the abdominal wall, an abdominal binder, and of gastric inflation on intraperitoneal pressure. The cross-bar indicates the mean intraperitoneal pressure before, and the arrow point the mean pressure after, the manipulation of the abdominal wall or inflation of the stomach.

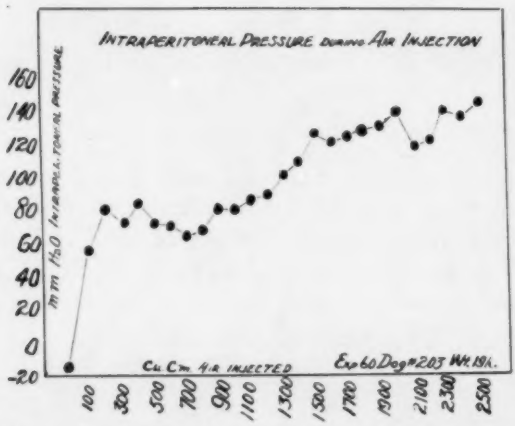

Fig. 9.—Graph showing the effect on intraperitoneal pressure of repeated injections of 100 cc. of air into the peritoneal cavity. Note the stationary pressure valves after the first 100 cc. was injected.

(fig. 9). Air in greater amounts than 100 cc. per kilogram of body weight could be injected into the peritoneal cavity before proportional increases in the intraperitoneal pressure followed the additional injections of greater volumes of air.

In the presence of pneumoperitoneum, various manipulations of the abdominal wall or inflation of the stomach by an intragastric balloon caused more marked shifts in the intraperitoneal pressure than was found when the air was not present within the peritoneal cavity (fig. 10).

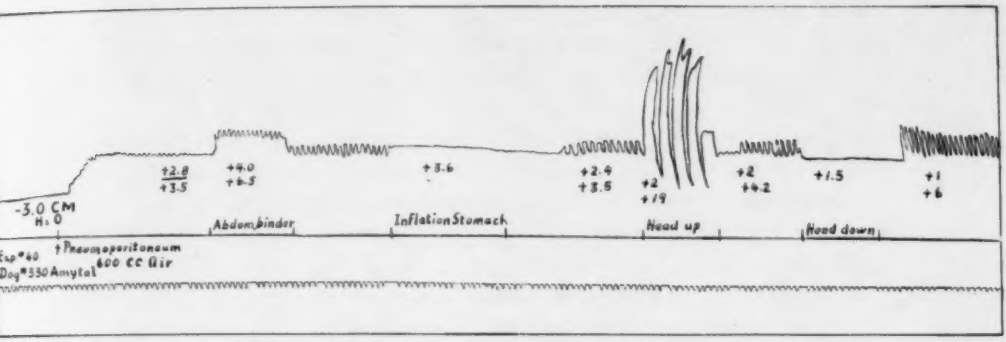

Fig. 10.—A kymographic tracing showing the effect of the intraperitoneal injection of 600 cc. air in a dog weighing 9 Kg. Note the effects of various changes in position and manipulation of the abdomen.

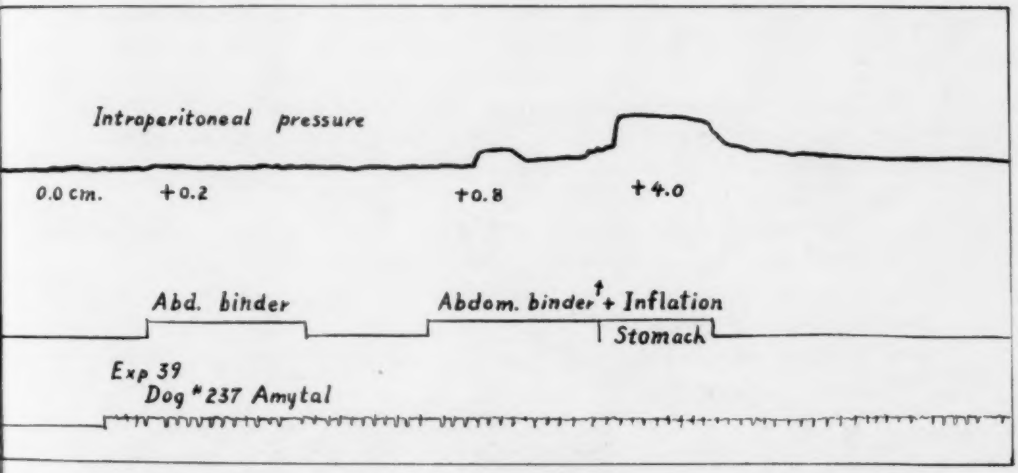

Fig. 11.—A kymographic tracing showing the slight effect that an abdominal binder has on the intraperitoneal pressure. Note the rise of pressure when a binder and gastric inflation were carried out simultaneously. Note the absence of respiratory excursions by this method.

COMMENT

The pressure within the peritoneal cavity is extremely variable. The relative positions of the cannula and the trunk of the dog determine whether the intraperitoneal pressure value is greater or less than atmos-

pheric pressure. The pressure is greatest in the most dependent portions and lowest in the uppermost portions. Our observations would tend to substantiate the conception of Krause [1] that the hydrostatic pressure of the contents of the abdominal cavity together with the flexibility of a portion of the abdominal walls determine, for the most part, the pressure within the abdominal cavity. The abdomen must be considered as an air-tight space so that, without outside communication, shifts in the position of the contained viscera effect a variation of the pressure in the upper portions of the peritoneal cavity. This decrease in pressure is sufficient to maintain a value below atmospheric pressure in the upper part of the abdomen with the animal in the horizontal or erect position.

In addition to the hydrostatic factor of the movable viscera, the alteration in the size of the abdomen incident to the phases of respiration is the second most important factor in the consideration of intraperitoneal pressure. In contradistinction to the reports of numerous other investigators, we were unable to observe an increase in pressure during inspiration with the animal breathing quietly in any position. On the contrary, we found that the intraperitoneal pressure was lessened during inspiration and attained its greatest value during expiration. We would conclude from this that the excursion of the costal arches and the increased distensibility (relaxation of the muscles) which occurs during inspiration more than compensates for the descent of the diaphragm. Since the subatmospheric pressure in the upper part of the abdomen is dependent on a sagging or "giving way" of the flexible walls below, it seems plausible that the relaxation of the abdominal muscles during inspiration is an important factor in the inspiratory decrease of pressure in the upper part of the abdomen.

The fact that the pressure within the peritoneal cavity decreases simultaneously with the decrease in intrapleural pressure (during inspiration) suggests the close relationship between abdominal activity and respiration. It also suggests the possibility of interference with pressure variations above the diaphragm by the opening of the sealed cavity below.

The ability of the abdominal walls and diaphragm to adjust themselves to conditions tending to raise the intraperitoneal pressure is shown by the minor shifts in pressure incident to the application of abdominal binders or distension of the stomach. The fact that the mean intraperitoneal pressure rarely exceeded atmospheric pressure even after gastric distention suggests the importance to respiratory and diaphragmatic activity of the maintenance of subatmospheric pressures in the immediate subdiaphragmatic region.

The immediate shift in the intraperitoneal pressure following the injection of small amounts of air and the very slow subsequent increase

in pressure following further injection again point out the extreme flexibility of the abdominal walls. A similar observation was made by Coombs,[13] who noted pressure changes in the peritoneal cavity of cats during the injection of physiologic solution of sodium chloride. She found that the pressure did not increase in proportion to the fluid injected until a critical point was reached. This was explained on a basis of a reflex "postural activity" of the abdominal musculature.

13. Coombs, H. C.: The Mechanism of the Regulation of Intra-Abdominal Pressure, Am. J. Physiol. **61**:159 (June) 1920.

THE DIMENSIONS AND GROWTH OF THE PALATE IN THE NORMAL INFANT AND IN THE INFANT WITH GROSS MALDEVELOPMENT OF THE UPPER LIP AND PALATE

A QUANTITATIVE STUDY *

WILLIAM T. PEYTON, M.D.
MINNEAPOLIS

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The investigator should consider himself fortunate if he finds a field of investigation in which opinions and estimates have long been expressed and in which more recently the fundamentals have been subjected to debate in a tone of controversy. He should be especially pleased if he takes up this subject with the intention of applying the comparatively newer quantitative methods of analysis and finds that these methods have not yet been tried in this particular field, although they are well suited for it.

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* From the Department of Surgery, University of Minnesota.

Investigation of the quantity and position of the tissue in children with cleft palate answers the foregoing hypothesis. For years opinions have been expressed to the effect that there is a deficiency of tissue in cases of congenital clefts of the upper part of the face and jaw. Brophy (1907) brought controversy when he said that all tissues are present. Since this statement was made, it has been refuted by opinions based on clinical estimates or made on a few measurements, taken for the most part on the facial skeleton rather than directly on the palate.

The solution of this question, namely the amount and disposition of the tissue in the cleft palate, is essential to the selection of plans for the surgical repair of these clefts. Fundamentally, there are three principal types of operation typified by the operations of Krimer, Warren and Brophy for clefts of the alveolar process and palate, all of which have undergone many modifications by other surgeons. The operation of Krimer, better known as the flap operation of Lane, is similar to other plastic flap operations in general surgery used to restore defects which are due to loss of tissue. The Warren-von Langenbeck operation

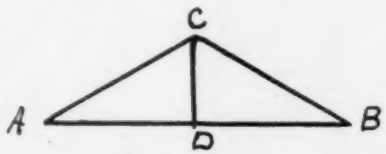

Fig. 1.—Measurements of palate as they were determined by Alkan.

is similar to other plastic operations performed for the restoration of defects caused by separation, but without loss of tissue. The Brophy operation is based on the assumption that the cleft is due to lateral separation of normally developed tissue.

This study is undertaken with no attempt to prove any expressed opinion or to support a personal theory.

LITERATURE

THE NORMAL PALATE

Quantitative growth of the normal palate has been subjected to only superficial investigation. Alkan measured the width and length of the hard palate with a calipers, and calculated the height. He took the diameter or width (fig. 1, *AB*) between the first and second premolar and also between the first and second molar teeth from the inner margin of the gum, except in new-born children where only one measurement of the width was taken, and this at approximately the middle of the alveolar process. From this same point on each side of the alveolar process, he took measurements *AC* and *CB* (fig. 1) where *C* is located

at approximately the center of the arch of the palate. The height of the palate *CD* was then calculated from the known values for *AC*, *CB* and *AB*.

The material measured by Alkan included thirty-five infants from 1 to 9 days of age and also one child 90 days old. No trend of growth is demonstrated in these measurements. The averages were as follows: width, 2.7 cm.; length, 3.2 cm., and height, 1.2 cm. He computed width-height indexes to compare with similar indexes computed for adult

TABLE 1.—*Dimensions of Palates of Children as Determined by Alkan*

Age, Days	Sex		Skull			Palate		
	Male	Female	Length, Cm.	Width, Cm.	Width of Face, Cm.	Width, Cm.	Length, Cm.	Height, Cm.
1	..	1	11.7	8.8	7.0	2.6	3.4	1.5
1	1	..	12.1	9.1	7.3	2.6	3.1	1.0
1	..	1	11.9	9.7	7.1	2.8	3.4	1.05
1	..	1	12.0	9.4	7.2	2.9	3.4	1.3
2	..	1	9.7	8.0	5.85	2.1	3.2	0.8
2	..	1	11.6	9.0	6.5	2.5	3.2	1.2
3	..	1	11.6	9.5	7.3	2.9	3.5	1.3
3	..	1	11.2	8.3	6.6	2.6	3.3	1.3
3	..	1	12.0	8.8	7.1	2.8	3.0	0.95
3	..	1	11.5	9.3	7.1	2.7	3.1	1.4
3	..	1	11.9	9.0	7.1	2.4	3.4	1.3
3	..	1	11.8	9.7	6.9	2.4	2.9	1.3
4	1	..	10.7	8.6	6.4	2.3	3.1	0.9
4	..	1	12.0	8.9	6.8	2.4	3.3	0.8
4	1	..	11.6	8.8	7.2	2.7	3.1	1.4
4	1	..	13.0	9.8	7.3	3.0	3.1	1.1
4	..	1	11.3	8.5	6.9	3.0	2.9	1.0
4	..	1	11.7	9.2	7.4	2.8	3.3	1.4
5	1	..	11.6	9.3	6.8	3.1	3.5	0.9
5	1	..	11.5	9.3	7.2	2.9	3.2	1.3
5	1	..	11.9	9.0	6.6	2.6	3.0	1.1
5	1	..	11.6	8.6	6.7	2.8	3.0	1.3
6	..	1	11.3	9.3	7.2	2.6	3.6	1.2
6	..	1	10.5	7.6	6.5	2.5	3.4	1.1
6	1	..	12.0	9.0	7.2	2.6	3.2	1.3
6	1	..	11.4	8.8	7.2	2.8	3.3	1.3
7	1	..	12.2	9.6	7.3	3.0	3.3	0.95
7	1	..	11.7	9.3	7.5	2.8	3.0	1.1
8	1	..	11.9	9.0	6.7	2.5	3.2	1.1
8	..	1	11.7	8.9	6.9	2.7	3.0	1.1
8	1	..	13.1	9.4	7.2	2.9	3.5	1.3
8	1	..	12.3	10.4	7.3	3.0	3.4	1.3
9	..	1	11.4	9.1	6.5	2.6	3.0	1.0
9	..	1	11.9	8.9	7.0	2.6	3.1	1.3
9	..	1	12.1	9.6	7.4	2.9	3.2	1.3
90	1	..	11.2	8.7	6.2	2.8	2.9	1.1

material and concluded that the palate of the new-born infant is relatively short and high. His measurements are recorded in table 1.

Denzer took some measurements on the palates of children under 1 year of age by making impressions of the palate, and from these impressions he made dental casts. Measurements were read from the dental cast with the surveying apparatus of Stanton. This surveying apparatus is an orthoscopic apparatus with which it is possible to locate and read the position of a point in three dimensions. It is therefore used to make orthographic projections from models and for measuring elevations. For width, Denzer took the widest point of the alveolar process, and for height the highest point of the arch of the palate.

These are the same measurements which have been taken in the present investigation. The results as determined by Denzer are recorded in tables 2 and 2*a*. The averages of his measurements were width, 30.9 mm. and height, 8.79 mm.

W. K. Connell read a paper before the Anatomical Section of the British Medical Association in 1922 on the "Form of the Palate in Children." He took an impression of the upper dental arcades in plasticine and studied the variations in shape and determined in normal and abnormal conditions the changes which took place during growth,

TABLE 2.—*Dimensions of Palates of Children as Determined by Denzer*

Age	Greatest Width, Mm.	Greatest Height, Mm.	Age	Greatest Width, Mm.	Greatest Height, Mm.
3 months	32.5	8.7	5 months	32.0	8.2
4 weeks	27.5	8.0	5 months	30.5	10.0
4 weeks	29.0	8.0	5 months	30.0	8.6
12 days	30.0	11.3	5 months	28.5	9.0
6 weeks	28.5	8.0	6 months	31.5	9.7
6 weeks	30.0	9.9	6 months	30.5	8.6
6 weeks	30.5	9.6	6 months	28.5	7.2
7 weeks	28.0	7.4	7 months	31.5	7.7
2 months	28.0	9.5	7 months	30.0	8.7
2 months	27.0	7.7	7 months	32.0	8.1
2 months	31.0	10.1	8 months	33.5	8.3
2 months	28.5	7.5	8 months	31.5	9.9
3 months	32.0	7.4	9 months	35.0	8.0
3 months	32.5	8.7	9 months	32.5	7.1
4 months	33.0	9.7	10 months	36.0	9.3
4 months	32.0	9.4	11 months	30.0	9.5
4 months	30.0	8.7	11 months	34.0	9.4
4 months	34.0	9.5	11 months	33.0	8.1
4 months	32.5	10.0			

TABLE 2a.—*Average Dimensions at Different Ages*

Age	Number of Cases	Greatest Width, Mm.	Greatest Height, Mm.
1 to 3 months, inclusive	13	29.4	8.7
4 to 6 months, inclusive	12	31.0	9.0
7 to 11 months, inclusive	11	32.6	8.5
All children under 1 year	29	30.9	8.89

also the relation of the size of the arch to the state of development of the child. He found that, "There was no connection between the size of the child and the shape of the palate, nor was there any alteration in the arcade in children with adenoids."

Buser measured the width, height and length of the palate in 514 persons all of whom were over 15 years of age. He used special instruments, with which he took readings directly from the palate, without the use of impressions or casts. Two measurements of width were taken: one at the first premolar tooth and the other at the first molar tooth. Height was taken as the highest point of the arch of the palate in relation to the occlusive surface of the teeth. Length of the palate was taken as a direct line measurement from the space between

the medial incisors in front to the posterior edge of the hard palate. Division according to sex was made in all of his tables, and still further divisions according to age were made in some of his tables. The data on persons from 15 to 17 years of age are included in one table, and on all above this age are included in the second table. The male palate in each of its dimensions is approximately 1 mm. greater than those of the female, according to his observations, and there is a slight increase in size after the fifteenth year. The approximate dimensions of the adult palate taken from the tables of Buser are as follows: width (at first molar), 48 mm.; height, 21 mm. and length, 54 mm. Table 3 is copied from Buser.

Shaw measured the width, height and length of the palate in adults. His results were: height, 14.2 mm.; length, 50.8 mm., and width (at first molar), 35.5 mm.

TABLE 3.—*Dimensions of Palates as Determined by Buser*

Age of Individuals Measured	Dimension	Males		Females	
		No. Cases Measured	Average Size, Mm.	No. Cases Measured	Average Size, Mm.
15 years of age and over	Palate width, first premolar	257	37.5	257	36.0
	Palate width, first molar....	213	48.6	186	46.9
	Palate height.....	257	21.6	257	20.2
	Palate length.....	254	54.7	257	52.7
15 to 17 years of age.....	Palate width, first premolar	17	37.7	75	35.7
	Palate width, first molar....	12	47.9	53	46.3
	Palate height.....	17	20.8	75	19.6
	Palate length.....	17	53.2	75	52.8
18 years of age and over	Palate width, first premolar	240	37.4	182	36.1
	Palate width, first molar....	201	48.6	133	47.2
	Palate height.....	240	21.7	182	20.4
	Palate length.....	237	54.8	182	52.7

Gustav Franke measured a large series of palates at different ages. The width of the palate, measured at the posterior border of the first molar tooth, as determined by Franke is as follows: 2 to 7 years, 41.1 mm.; 8 to 13 years, 45.9 mm.; 14 to 21 years, 48 mm.; 22 to 29 years, 49.4 mm.; 30 to 50 years, 50.2 mm. The length of the palate, according to Franke's figures, was 26.8 mm. at birth and 52.8 mm. in the adult, or approximately a twofold increase between birth and maturity.

THE MALDEVELOPED PALATE

Quantitative studies of growth and of the amount and disposition of tissue in the cleft palate are meager, but there are many opinions based purely on clinical observation or on the writings of others.

The measurements which have been taken to estimate the quantity of tissue or the spread of tissues in the palate have for the most part been taken indirectly; either skull measurements were taken to determine the breadth of the facial portion of the skull, or to determine the dis-

tance between the hamular process, or between other similar bony points of the facial skeleton. These measurements have been made largely on the macerated skull rather than on the living child.

Some measurements made by Kirkham on skulls in the Hunterian Museum of London are given in table 4. The greatest abnormality in dimensions of cleft palates according to these figures, is in the distance between the hamular processes.

Skull measurements, made by Wardill on museum specimens with and without cleft palate, together with similar measurements taken by Veau and quoted by Wardill are recorded in table 5. Wardill concluded from these measurements of the bony parts that there is associated with

TABLE 4.—*Skull Dimensions as Determined by Kirkham*

Age	Distance Between Posterior Palatine Foramina, Mm.	Distance Between Hamular Processes, Mm.	Distance From Hamular Process to Posterior Palatine Foramina, Mm.	Distance Between Tuberosities, Mm.
Normal children				
Birth	17.5	18.0	6.0	27.0
2 months	19.5	22.0	5.5	30.0
10 months	20.0	ns*	ns	30.5
8 months	22.0	22.5	7.5	29.5
12 months	23.0	23.0	9.0	33.5
19 months	22.5	ns	ns	35.0
2 years	21.5	ns	ns	33.0
2¼ years	23.0	ns	ns	37.5
2½ years	23.5	24.5	9.0	37.0
3 years	22.0	24.0	9.0	37.5
3½ years	22.5	27.0	10.0	36.5
4 years	22.0	29.0	12.0	39.0
5 years	25.0	27.5	12.0	36.0
5¾ years	15.0	28.0	11.0	37.5
6 years	22.5	ns	ns	37.5
8 years	27.0	32.0	12.0	40.0
Normal				
Average adult	30.0	34.0	12.0	54.0
Cleft palate				
Adult	40.0	41.0	12.0	54.5
Nubian woman	40.0	46.0	10.5	55.0

* Hamular process was missing and therefore measurement was not taken.

cleft palate a small but definite increase in the transverse diameter of the nasopharynx.

Izard has determined that there is a rather constant relationship in the adult between the transverse diameter of the palate and the bizygomatic diameter of the facial portion of the skull. This relationship is approximately 1 : 2, but it apparently does not hold for infants in which the bizygomatic distance is considerably less than twice the transverse diameter of the palate. The transverse diameter of the palate and the bizygomatic diameter of the skull, as determined by Ruppe, are included in table 6. Ruppe concluded that for infants these measurements of skulls with cleft palate are quite similar to those of normal skulls, and therefore, that there is no evidence of separation of the maxilla in the cleft palate.

Superimposing tracings of the alveolar curves of the maxilla and mandible, J. E. Thompson concluded that the maxillary tuberosities have not been much displaced in cleft palate, since he found the maxillary process at this point seldom more than 1 mm. greater than that

TABLE 5.—*Measurements Compiled by Wardill*

Nasion to Occipital Point, Mm.	Transverse Diameter, Mm.	Transverse Hamuli, Mm.	Nasion to Occipital Point, Mm.	Transverse Diameter, Mm.	Transverse Hamuli, Mm.
180.0	153.0	38.5	176.0	148.0	35.0
162.0	149.0	43.0	171.0	133.0	28.0
156.0	133.5	32.0	160.0	133.0	33.0
127.0	117.0	27.0	151.0	124.5	23.0
123.0	103.0	24.0	148.0	124.0	26.0
122.0	101.0	24.5	133.5	117.0	23.5
121.0	102.0	31.0	120.0	92.0	21.0
117.0	111.0	31.0	112.0	90.0	18.5
101.0	82.0	23.0	107.0	84.0	22.0
100.0	94.0	26.0	103.0	90.0	19.0
93.5	88.0	24.5	99.0	82.5	19.5
93.0	83.0	25.0	96.0	82.0	17.5
*Glabella to Occipital Point, Mm.			*Glabella to Occipital Point, Mm.		
175.0	128.0	41.0	178.0	149.0	34.0
187.0	150.0	42.0	190.0	147.5	36.0
187.0	145.0	43.5	195.5	191.5	32.5
169.0	125.0	39.5	180.0	141.0	30.0

* Glabella to occipital point substituted here for nasion to occipital point distance because in the skulls with cleft palate a large part of the calvarium had been removed.

TABLE 6.—*Skull Dimensions as Determined by Ruppe*

	Transverse Diameter of Palate, Mm.	Bizygomatic Diameter, Mm.	Twice the Bimaxillary Distance, Mm.
Skulls of normal infants.....	14	23	28
	16	26	32
	17	28	34
	17	30	34
	18	30	36
	19	33	38
	21	34	42
	25	46	50
	27	44	54
	27	48	54
	28	48	56
	33	56	66
	33	57	66
	35	62	70
Skulls of infants with cleft palate...	60	100	120
	48	85	96
	45	70	90
	32	78	64
	43	86	86
	40	66	80
	47	92	94
	50	82	100

of the mandible, but the most prominent curve of the alveolar processes he found 2 or 3 mm. displaced or spread.

Trendelenburg concluded that the facial portion of the skull is wider than normal when the palate is cleft. He took measurements on the width of the choanae, the distance between the infra-orbital foramen

and between the zygomaticomaxillary suture of each side on skulls with and without cleft of the palate, and found that these dimensions are greater in persons with cleft palate.

Alex Lindberg stated that measurements of normal patients and patients with cleft palate demonstrate the mesopharynx to be from 0.5 to 1.5 cm. greater in the latter.

Opinions based in part or entirely on observation, rather than measurement, are found in the literature on maldevelopments of the lip and palate. These opinions are readily divisible into two groups completely at variance with each other. In one group are those who believe that all the tissue is present, and in the other are those who believe there is an actual deficiency of tissue due to deficient development, arrested growth or atrophy. Outstanding among the former and apparently the first to press this opinion was Brophy (1907), who maintained that children who have congenital malformation of the palate, with rare exceptions, have the normal amount of tissue in the palate. Brophy maintained that when the margins of the cleft have been brought into contact, the upper jaw is then restored to its normal breadth and to its proper relation to the lower jaw. There are few exceptions, and he further said that other writers have been unconscious of the fact that as a rule the bones are not deficient in structure or incomplete in development.

Veau also expressed the belief that the parts are normal, or if less than normal, that they have between them the ability to reproduce the normal amount of palate tissue. He stated that they are developed as a normal palate, but that it becomes abnormal only because of lack of coalescence.

The opinion of the majority falls in the second group, which holds that there is not a normal amount of tissue in the cleft palate.

Arthur Keith (1909) quoted Brophy to the effect that there is no deficiency in the tissue of the cleft palate. But Keith stated that this was not the case in the specimens that he had examined. He examined the palates of three adults with clefts and found the clefts on the average 20 mm. wide; the average breadth of the palate was 64 mm., and this, he said, demonstrates that the bony parts of these palates were from 10 to 15 mm. less than normal. In new-born children, according to Keith, the deficiency affects the inner or marginal area of the palate but it does not amount to more than 3 mm. on each side. He admitted that he is not able to say whether or not the cleft continues to increase after birth, but judging from the width of the cleft of the adult palate, he concluded that they do not continue to separate at the rate after birth that they did before birth.

Winternitz is of the opinion that the halves of the cleft palate are rudimentary, and that their relative growth is not in proportion to that

of the oropharyngeal cavity, wherefore in later years the cleft is not only wider, but that this lack of development causes a relatively short soft palate after repair, and therefore is the cause of poor speaking function after repair. He is of the opinion that this lack of development in relation to the skull is especially marked in the soft palate.

According to Trendelenburg, there is a lack of normal development not only of the palate on the side of a unilateral cleft, but the growth of the entire jaw on this side is retarded. Failure to recognize the short side of the alveolar process as a part and not a complete half of the process is apparently the basis of this opinion.

Ernest Frazer said there is no question that an extra protrusion of the frontonasal region and elongation of its septal portion does occur, but it is possible that a certain amount of the appearance of protrusion is really due to a deficiency of the maxillary mass placed beside it. He is of the opinion that "accurate measurements, however, under many conditions are necessary in quantity."

Wardill, in speaking of the cleft palate, said, that there is less than the normal amount of soft tissue, and that this has been used to bridge an abnormally wide nasopharynx. J. F. Esser said that one should not forget that there is practically always a deficit of material.

COLLECTION OF DATA

MEASUREMENTS TAKEN

The data consist essentially of two parts: (1) general body and head measurements and (2) palate measurements. Weight and standing and sitting height were the general body measurements taken. Twenty-three head measurements were taken, but are not all incorporated in this report; seven of these head measurements were bilateral. Crown-heel length and fronto-occipital diameter are the only body and head measurements used in this report. The body and head measurements were taken in the usual manner. Details of procedures in obtaining those used in this study are given in the following paragraphs. Special technic for obtaining palate measurements were worked out, the details of which are subsequently given.

METHOD OF OBTAINING MEASUREMENTS

The crown-heel length was taken with the Martin anthropometer, the straight attachments being used, and the frontal-occipital diameter was taken with Martin curved arm calipers.

All the measurements on the palate were taken from dental casts and dental molds. Kerr perfection impression compound was used to make these dental casts. A dental tray could not be found on the market small enough to use in the first year of life. To obtain a suitable tray, an impression was made of the upper jaw of a new-born infant, and a dental tray was made up from this.

The impression compound was softened in warm water and applied to the palate on the dental tray; cold water on a sponge was applied to harden the material quickly before its removal from the mouth. These impressions were flowed up in dental plaster of paris in the usual manner to obtain a plaster of paris mold (dental cast) of the palate. One of the most difficult points to determine was the medial edge of the palate plate in cases with cleft. As a rule, however,

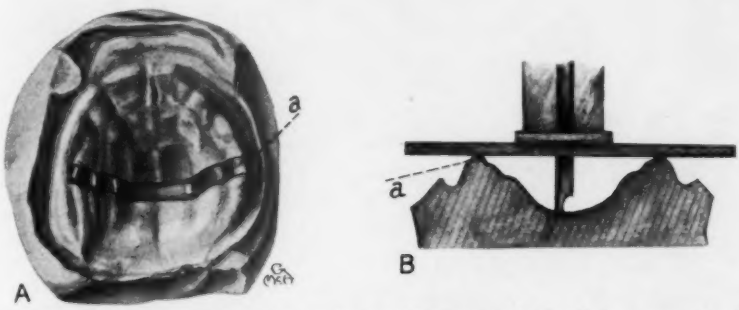

Fig. 2.—Method of taking the surface width and height of the normal palate. In *A*, the lead foil is applied at the widest part of the alveolar process to obtain the surface width of the palate. *B* is a cross-section of the palate to show the method of measuring the height of the palate. *a* shows measurement at the highest point of the alveolar process.

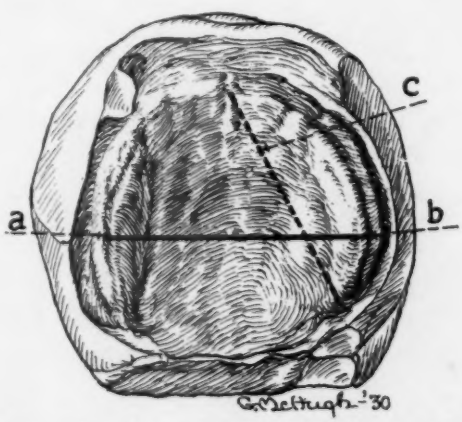

Fig. 3.—Measures taken for the normal palate: *a*, the widest transverse diameter of the palate measured to the highest point of the alveolar process (*b*); *c*, the chord of the alveolar process.

this was well demarcated by a line representing the transition from the squamous epithelium of the oral cavity to the ciliated epithelium of the nasal cavity.

Four dimensions common to both the normal and maldeveloped palate were taken, and in addition, the width of the cleft was read in the maldeveloped palates. Those common to both the normal and the cleft palate were: (1) widest transverse diameter, (2) surface width of palate, (3) height of palate and (4) the chord of the alveolar process which is referred to in the text as the length of

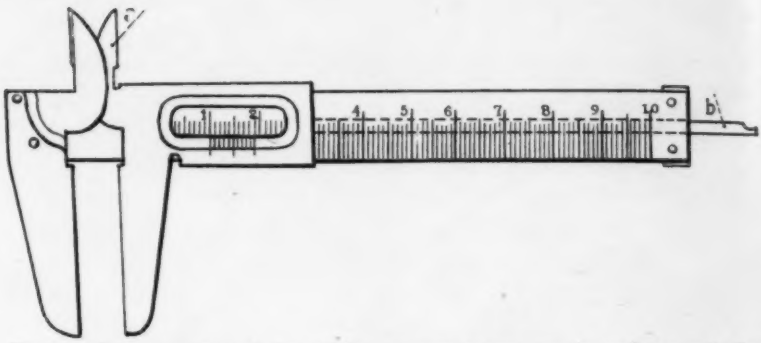

Fig. 4.—Instrument used for taking measurements on the palate: *a* indicates the blade used for measuring the width of the cleft, and *b*, the sliding bar used for measuring the height of the palate.

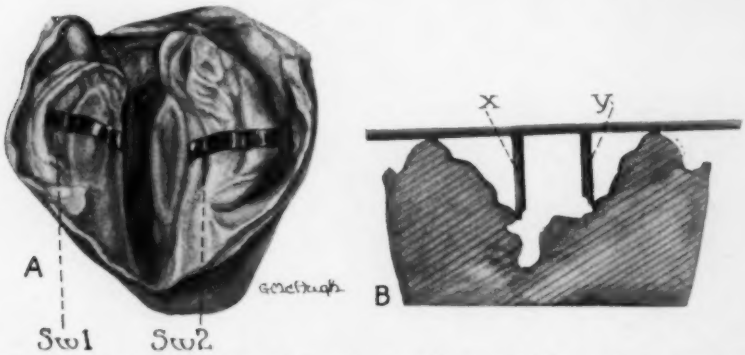

Fig. 5.—Method of taking the surface width and height of the palate in unilateral clefts of palate. In *A*, *Sw* indicates the surface width of the palate; Sw1 + Sw2 = total Sw. *B* is a cross-section of the palate; $\frac{X+Y}{2}$ = height of palate.

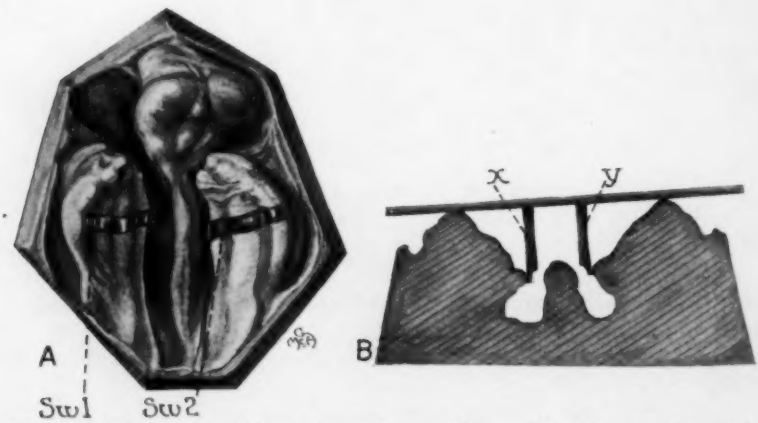

Fig. 6.—Method of taking the surface width and height of the palate in bilateral clefts of the palate. In *A*, Sw indicates the surface width of the palate; Sw1 + Sw2 = total Sw. *B* is a cross-section of the palate; $\frac{X+Y}{2}$ = height of palate.

alveolar process. The method of taking these measurements in the normal palate is illustrated in figures 2 and 3, and for the cleft palate in figures 4, 5, 6 and 7.

In general, the descriptive name designates what these measurements are, but the end-points utilized and the exact method of taking them is as follows: The widest transverse diameter of the palate was taken in approximately the coronal plane, using the middle of the alveolar process as end-points. The surface width

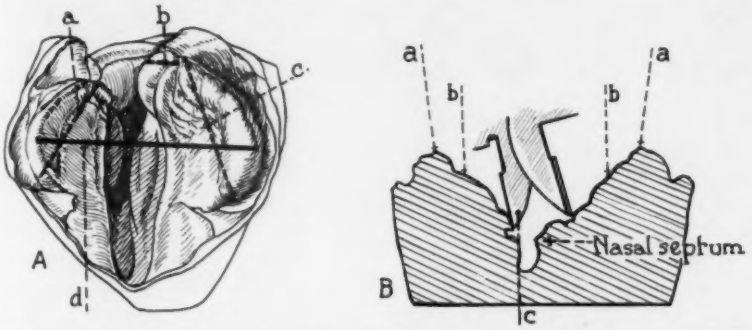

Fig. 7.—Measures taken for the widest transverse diameter, length of the alveolar process and the width of the cleft in unilateral clefts of the palate. In *A*, $a + b$, and *c* indicates the chords of the alveolar process; *d*, the widest transverse diameter of unilateral cleft palate. In *B*, *a* indicates the alveolar process of the palate; *b*, the plate of the palate, and *c*, the method of measuring the width of unilateral cleft palate.

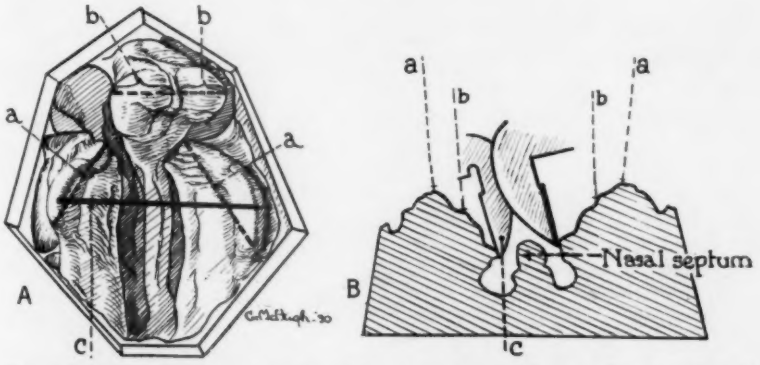

Fig. 8.—Measures taken for the widest transverse diameter, the length of the alveolar process and the width of the cleft in bilateral clefts of the palate. In *A*, $a + b$ indicates the chord of the alveolar process, and *c*, the widest transverse diameter of a bilateral cleft palate. In *B*, *a* indicates the alveolar process of the palate; *b*, the plate of the palate, and *c*, the method of measuring the width of a bilateral cleft palate.

of the palate was taken in approximately the same coronal plane as the widest transverse diameter and with the same end-points but in the following manner. Thin sheet lead was cut into strips from 1 to 2 mm. wide, and this strip pressed firmly against the palate so that it assumed the shape of the palate surface includ-

ing all its irregularities. After the strip had been so pressed into position, it was cut at the end-points of the measure, that is, where the strip passed over the mid-portion of the alveolar process. The strip was then removed, pressed out on a flat surface to remove all irregularities, and with a calipers this straight piece of metal was measured. This dimension is referred to as the surface width of the palate. In the cleft palate, two strips were used, one for each plate of the palate, and here the end-point for the medial edge of the plate was taken at the point of transition of the squamous epithelium of the oral cavity into the ciliated epithelium of the nasal cavity.

The height of the palate was taken by placing a rigid metal bar across the palate at its deepest portion, and the distance from the upper surface of this metal bar to the deepest point of the mold was read. The width of the transverse bar was subtracted from this reading and the remainder taken as the actual height of the arch of the palate. A true curvelinear measurement of the length of the alveolar process was not taken, but instead a straight line measurement, the arc of the alveolar process was measured to estimate its length. It was taken from the midpoint anteriorly to the posterior end of the alveolar process on each side. The measurement for each side was recorded separately, but the average of both sides has been used in this analysis. This measurement could not be taken directly on the short side of the unilateral clefts, nor directly on either side of the bilateral cleft, but was, in the unilateral cases, taken as the sum of the short side plus one-half the width of the premaxilla, and in the bilateral clefts as the length of one side plus one-half the premaxilla. The width of the cleft was taken with a calipers as illustrated in figure 3, at the point of the widest separation of the medial edge of the plates of the palate.

SELECTION OF MATERIAL

The material consists essentially of two groups, namely, normal children and maldeveloped children, each group covering approximately the same growth period.

Ninety-one normal children are included in this material, fifty-one of whom are females and forty are males. This division as to sex was entirely chance since no attempt was made at selection. In age they ranged from a new-born (premature) infant to a child 362 days of age and in length from 45.7 cm. crown-heel length (a premature infant) to 75.7 cm. crown-heel length. All were presumably normal children. They were obtained from (1) the Out-Patient Dispensary at the University Hospital, (2) the Infant Welfare Clinics of Minneapolis, (3) various homes for illegitimate children and (4) hospital boarders. Physically abnormal children were not accepted for measurement.

In collecting the maldeveloped material, only children with complete clefts of both the alveolar process and hard and soft palate (that is, group III according to the Ritchie-Davis classification) were accepted. One exception to this general rule was made; this was a chld with a complete unilateral cleft of the lip and process, but with a normal hard palate and soft palate. Twenty-six abnormal cases were obtained, and two of these were measured twice, with an interval of several weeks between measurements. This makes a total of twenty-eight sets of measurements, and represents the material coming to the University Hospital between January, 1928, and March, 1930, and in addition, eight others who were during this period private patients of Dr. Ritchie. Included in this abnormal material are six females and twenty males, varying in age from a premature infant to a

child 425 days of age and in length from 47.5 cm. crown-heel length (a premature infant) to 75.1 cm. crown-heel length. The maldeveloped material is listed in table 7. The arrangement of this table is according to increasing crown-heel length, for the males, and females, respectively.

DATA LISTED

All data are listed in table 8. Division of the material is here made into normal and maldeveloped children, and each of these groups are divided according to sex. The order of listing is according to increasing crown-heel length. Age in days and weight in grams are included in this table, although they were not utilized in the present analysis of this material.

TABLE 7.—*Maldeveloped Children*

Crown-heel Length, Cm.	Age, Days	Description of Lesion
		Males
47.5	11*	Bilateral complete cleft of lip, process and palate
50.0	10	Right complete cleft of lip, process and palate
50.3†	8	Bilateral complete cleft of lip, process and palate
50.9	58	Left complete cleft of lip, process and palate
51.4	42	Left incomplete cleft of lip; complete cleft of process and palate
51.6‡	16	Right incomplete cleft of lip; complete cleft of process and palate
51.7	47	Right unilateral complete cleft of lip, process and palate
52.0	47	Right unilateral complete cleft of lip, process and palate
52.1	28	Bilateral complete cleft of lip, process and palate
52.3†	25	Bilateral complete cleft of lip, process and palate
52.7	46	Bilateral complete cleft of lip, process and palate
53.6‡	40	Right complete cleft of lip, process and palate
56.8	56	Left incomplete cleft of lip and process;complete cleft of palate
56.9	121	Right complete cleft of lip, process and palate
56.9	21	Left complete cleft of lip, process and palate
57.0	71	Right complete cleft of lip, process and palate
57.8	89	Left complete cleft of lip and process; incomplete cleft of palate
59.0	76	Bilateral complete cleft of lip, process and palate
59.2	101	Right incomplete cleft of lip; complete cleft of process and palate
59.5	110	Bilateral right complete cleft of lip, process and palate; left incomplete cleft of lip, process and palate
63.4	190	Left complete cleft of lip, process and palate
75.1	391	Left complete cleft of lip, process and palate
		Females
52.2	41	Right incomplete cleft of lip; complete cleft of process and palate
52.8	71	Bilateral complete cleft of lip, process and palate
58.9	81	Left complete cleft of lip, process and palate
59.7	95	Left incomplete cleft of lip; complete cleft of process and palate
63.7	246	Right complete cleft of lip, process and palate
66.1	186	Left complete cleft of lip, process and palate

* Premature infant.
† and ‡, same child measured a second time.

ANALYSIS OF DATA

TEST FOR NORMALITY

It is, of course, essential that the dimensions of the cleft palate be compared with the dimensions of the palate in normal children of approximately the same size. To check this, all the material, both normal and abnormal, was compared with a much larger series of normal children (approximately 600) collected by Dr. L. Richdorf.[1] They were

1. Richdorf, L.: A Quantitative Study of Growth of the Normal Infant in the First Year, unpublished thesis for degree of Doctor of Philosophy, University of Minnesota.

TABLE 8.—*Table of Data*

Crown-Heel Length, Cm.	Age, Days	Weight, Gm.	Fronto-occipital Diameter, Cm.	Widest Transverse Diameter of Palate, Cm.	Actual Surface Width of Palate, Cm.	Height of Palate, Cm.	Length of Alveolar Process, Cm.
			Males (Normal)				
49.0	2	3,020	11.1	3.00	3.50	0.72	2.90
49.2	1	3,355	12.3	3.20	3.90	0.93	2.98
49.3	16	3,015	12.0	3.25	3.90	0.97	3.05
51.5	4	3,115	11.7	3.27	3.80	0.94	2.70
51.7	16	3,484	11.7	3.38	3.81	0.96	3.07
52.1	14	3,555	12.6	3.30	3.90	0.98	3.25
52.6	53	3,975	12.5	3.20	3.70	0.81	3.00
52.7	0	3,760	11.2	3.40	3.80	0.81	3.17
52.9	6	3,160	12.2	3.40	3.85	0.80	2.98
53.4	5	4,105	12.1	3.45	4.00	0.80	2.90
53.7	66	4,020	12.5	2.90	3.40	0.71	2.70
54.2	20	3,960	12.6	3.00	3.70	0.94	3.05
54.3	36	4,000	13.5	3.42	4.00	0.86	3.15
54.6	37	4,705	13.1	3.45	4.20	0.85	3.28
56.6	48	4,945	11.7	3.35	4.10	0.96	3.20
56.8	86	4,845	....	3.32	3.90	0.87	3.10
57.9	87	4,760	12.7	3.10	3.80	0.93	2.78
58.9	124	6,170	13.3	3.60	4.20	0.91	3.18
59.0	119	5,675	12.6	3.20	4.30	0.85	3.00
59.0	136	5,595	13.8	3.50	3.65	1.00	3.05
59.3	45	5,429	13.8	3.60	4.30	0.93	3.28
59.9	105	6,790	11.8	3.50	4.25	1.04	3.25
60.1	113	4,750	13.4	3.35	4.00	0.86	3.18
60.4	101	6,505	13.8	3.42	3.80	0.79	3.28
60.5	93	5,670	13.3	3.55	4.35	1.01	3.35
61.7	140	7,045	14.0	3.40	4.00	0.91	3.25
62.9	141	6,255	13.4	3.42	4.22	1.12	3.38
63.6	123	6,805	12.7	3.60	4.00	0.72	3.25
64.1	135	6,275	13.2	3.40	4.02	0.84	3.53
65.1	219	8,340	15.3	3.40	3.90	0.76	3.24
65.7	198	7,300	13.4	3.60	4.17	0.95	3.17
65.7	141	7,810	....	3.70	4.40	0.96	3.55
66.6	168	6,700	12.6	3.70	4.30	0.94	2.95
66.8	225	8,630	14.2	3.60	4.32	1.00	3.36
67.0	179	7,850	12.8	3.60	4.50	1.17	3.00
68.0	286	7,571	14.0	3.50	4.20	0.99	3.41
69.0	313	9,695	14.5	3.70	4.50	1.07	3.58
69.3	238	8,625	15.2	3.60	4.35	1.00	3.20
72.5	330	10,433	15.4	3.40	4.25	1.00	2.85
75.4	250	9,800	16.1	3.60	4.05	0.72	3.33
			Females (Normal)				
45.7	10	2,380	11.1	2.75	3.20	0.84	2.70
48.8	12	2,885	11.7	2.90	3.30	0.72	3.05
49.3	10	3,640	11.7	3.50	3.60	0.85	3.00
50.0	29	3,220	12.5	3.00	3.80	0.85	2.90
50.2	3	3,050	11.5	3.00	3.60	0.80	2.78
50.4	10	2,900	11.4	3.10	3.65	1.04	2.73
51.8	10	3,230	11.6	3.10	3.50	0.77	2.95
52.5	40	3,850	13.7	3.45	3.80	0.84	3.05
52.7	66	3,925	12.4	2.81	3.45	0.87	2.71
53.1	35	3,783	12.6	2.90	3.30	0.72	3.00
53.1	32	3,630	11.5	3.20	3.72	0.81	3.11
55.2	36	3,769	13.0	3.00	3.71	1.13	2.85
55.4	47	3,945	12.1	3.30	3.85	0.87	3.25
55.6	60	4,645	12.4	3.10	3.90	0.97	2.95
56.1	63	5,215	....	3.05	3.65	0.84	3.23
56.3	158	5,475	13.2	3.32	4.40	0.90	3.18
56.3	68	5,144	12.8	3.20	3.65	0.82	2.82
57.3	51	5,600	12.5	3.30	4.00	0.91	3.28
57.5	91	5,130	13.0	3.40	4.00	0.97	3.30
57.9	83	5,157	14.2	3.20	4.00	0.94	3.10
58.2	82	5,606	13.4	3.00	3.70	0.97	3.05
58.5	85	6,105	12.4	3.50	4.10	0.92	2.97
58.7	83	.....	12.3	3.30	3.90	0.99	3.20
59.0	75	5,016	12.5	3.10	3.92	0.97	3.02
59.5	143	6,350	12.6	3.32	3.90	0.91	3.43
60.3	99	5,820	12.2	3.30	4.20	1.11	3.43
60.5	79	4,663	14.1	3.05	3.90	1.11	2.85
60.8	106	5,298	13.0	3.65	4.10	0.96	3.28
61.0	152	6,255	14.8	3.25	4.00	0.90	3.10
61.1	90	4,990	12.7	3.30	4.00	0.91	3.25
61.7	134	5,490	13.8	3.35	3.85	0.89	3.15
61.8	162	6,350	13.8	3.70	4.40	1.07	3.28
61.9	109	6,090	14.4	3.20	3.87	0.97	3.44
62.0	68	5,405	13.5	3.40	4.25	1.09	3.08

compared according to crown-heel length in relation to days in age, using graphic methods. The curves of Richdorf's data drawn through the mean for each month is depicted in figure 9 for the males, and in

TABLE 8.—*Table of Data—Continued*

Crown-Heel Length, Cm.	Age, Days	Weight, Gm.	Fronto-occipital Diameter, Cm.	Widest Transverse Diameter of Palate, Cm.	Actual Surface Width of Palate, Cm.	Height of Palate, Cm.	Length of Alveolar Process, Cm.
			Females (Normal)—Continued				
62.7	115	6,600	14.0	3.00	4.00	1.13	3.25
63.7	176	6,718	14.0	3.50	4.25	0.94	3.25
64.4	259	7,725	15.2	3.40	4.10	1.00	3.25
64.5	100	6,715	13.0	3.42	4.00	0.86	3.44
64.8	203	8,210	....	3.21	3.70	0.74	3.20
65.7	213	6,980	13.6	3.60	4.20	1.04	3.48
66.9	241	7,520	14.4	3.40	3.92	1.08	3.25
68.0	325	8,200	14.2	3.70	4.15	0.93	3.05
68.2	188	7,199	14.9	3.20	3.90	0.88	3.40
68.5	278	7,810	14.7	3.50	4.15	0.94	3.48
69.1	283	8,130	13.7	3.60	4.40	1.06	3.55
70.0	272	8,725	15.3	3.60	4.20	1.05	3.55
70.2	238	7,965	....	3.22	4.00	1.00	3.35
70.7	282	8,630	14.5	3.35	4.15	0.91	2.95
71.5	344	8,190	15.8	3.55	4.35	1.11	3.60
73.8	315	9,010	14.0	3.85	4.52	1.11	3.25
75.5	362	10,020	14.7	3.75	4.55	1.11	3.26

Crown-Heel Length, Cm.	Age, Days	Weight, Gm.	Fronto-occipital Diameter, Cm.	Widest Transverse Diameter of Palate, Cm.	Actual Surface Width of Palate, Cm.	Height of Palate, Cm.	Length of Alveolar Process, Cm.	Width of Cleft, Cm.
			Males (Maldeveloped)					
47.5	11	2,815	11.1	3.70	3.10	1.26	3.30	1.79
50.0	10	3,325	12.5	4.20	3.20	1.23	2.75	1.79
50.3	3	2,990	11.4	3.80	3.90	1.17	3.00	1.40
50.9	58	6,278	12.2	3.60	3.70	1.21	3.00	1.09
51.4	42	3,265	....	4.00	3.20	1.24	3.05	1.20
51.6	16	3,210	11.7	3.70	3.60	1.20	2.95	0.96
51.7	47	4,260	12.6	4.10	4.30	1.54	2.95	0.93
52.0	47	3,729	12.0	4.20	3.55	1.26	3.20	1.35
52.1	28	3,325	12.7	3.60	3.40	1.11	2.75	1.41
52.3	25	3,500	11.1	3.70	3.80	1.18	3.10	1.35
52.7	46	3,480	12.6	3.80	3.60	1.33	2.88	1.42
53.6	40	3,670	13.4	3.70	3.90	1.17	3.10	1.09
56.8	56	4,300	12.5	3.45	3.70	1.18	3.30	0.96
56.9	121	4,500	12.7	4.10	3.50	1.05	3.40	1.34
56.9	21	4,280	12.3	4.10	3.70	1.17	2.85	1.26
57.0	71	4,585	13.7	3.90	4.10	1.26	3.13	1.38
57.8	89	3,645	13.6	3.30	3.90	1.04	3.00	....
59.0	76	4,336	11.9	3.50	3.20	1.10	3.20	1.34
59.2	101	5,225	13.8	3.80	4.00	1.26	3.20	1.23
59.5	110	5,443	14.3	4.30	4.30	1.29	3.50	1.43
63.4	190	5,415	13.8	3.80	3.60	1.09	3.50	1.12
75.1	391	8,845	15.8	3.75	4.30	1.39	3.60	0.87
			Females (Maldeveloped)					
52.2	41	3,933	12.5	3.50	3.75	1.17	3.10	1.10
52.8	71	3,645	12.3	3.60	3.70	1.20	2.85	1.59
58.9	81	3,825	13.1	3.70	3.90	1.16	3.20	1.20
59.7	95	4,705	13.0	3.50	4.00	1.26	2.85	1.07
63.7	246	5,355	12.8	3.60	4.20	1.27	3.30	0.78
66.1	186	5,807	13.0	4.20	4.10	1.09	3.20	1.39

figure 10 for the females. Three times the probable errors of the means is indicated in each figure. Field graphs of the length with age of the present study are included in each figure, a difference in symbol indicating whether normal or maldeveloped. The children of this series are seen to be slightly smaller than those collected by Richdorf, especially

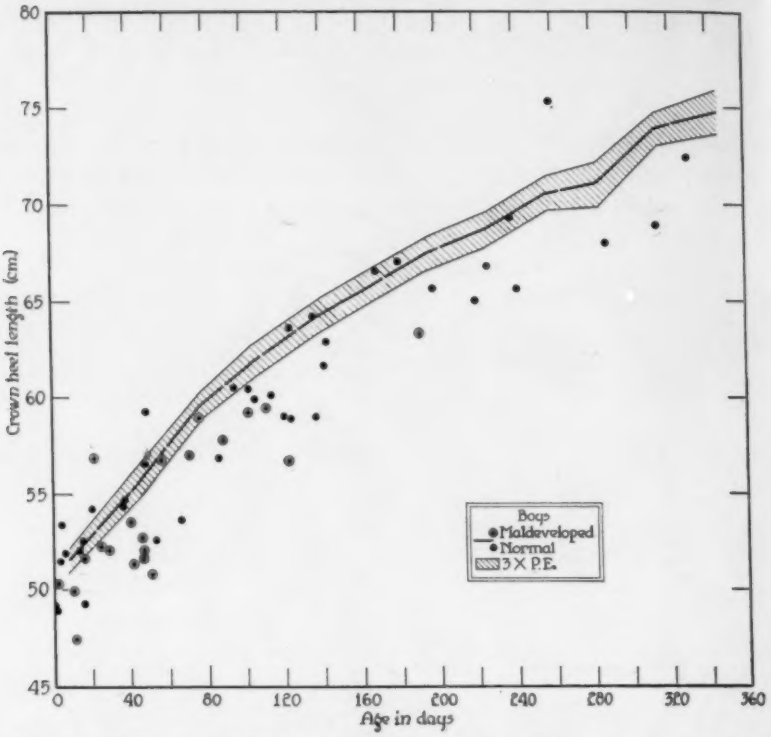

Fig. 9.—The curve of Richdorf's data for male children drawn through the mean for each month and field graphs of the length with age of the male children of the present study.

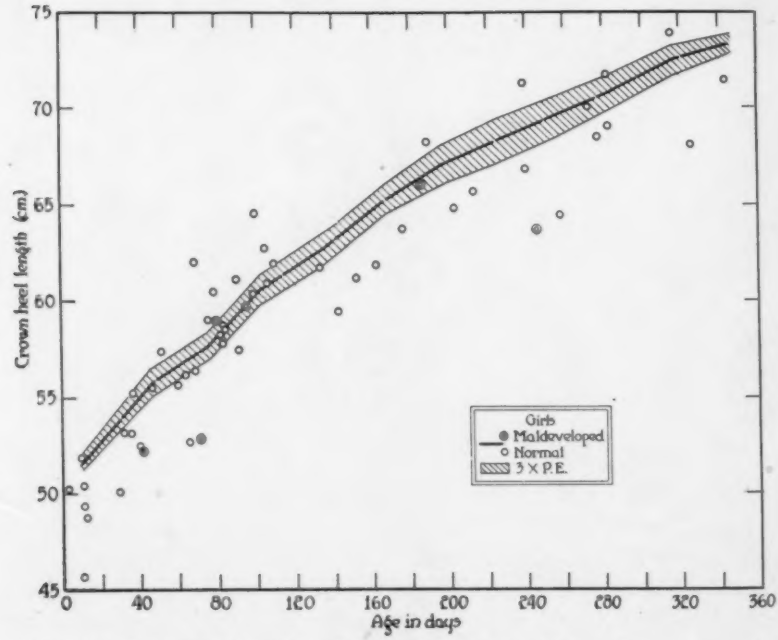

Fig. 10.—The curve of Richdorf's data for female children drawn through the mean for each month and field graphs of length with age for the female children of the present study.

is this true of the male children. The maldeveloped children, however, are approximately the same length for age and sex as the normal children of this series.

The question then arose whether or not the difference in length of males and females for the same age necessitated treating them separately according to sex. In a series as small as this it would be advantageous to combine boys and girls. In the pathologic series the males predominate approximately as 4.5 : 1, but in the normal material the females predominate as 5 : 4. Although in infancy, the female is smaller than the male, her bodily proportions are approximately the same. If this general rule holds for these data, they could be analyzed without regard to sex. For instance, if males and females of the same length have the same sized heads, the sex differences in length for age could be eliminated by using length instead of age as a base. To test this supposition, the trends of the fronto-occipital diameter with length were fitted by the method of least squares for both the normal boys and girls. This is the general method used throughout this study.[2]

Field graphs of the fronto-occipital diameter of the head with body length and their fitted trend are depicted in figure 11. The measures for male and female children are depicted in separate graphs with

---

2. D = difference between calculated and observed value of Y.

$$Y = BX + A$$
$$BX + A - Y = D$$
$$F = (BX + A - Y)\Sigma = \text{a minimum}$$

Differentiating with respect to B. $\frac{DF}{DB} = \Sigma(BX + A - Y)X = O$

Differentiating with respect to A. $\frac{DF}{DA} = \Sigma(BX + A - Y)1 = O$

Now solve the foregoing two simultaneous equations for B and A.

(1) $\Sigma X^2B + \Sigma XA - \Sigma YX = O$
(2) $\Sigma XB + \Sigma A - \Sigma Y = O$
(3) $\Sigma XY = \Sigma X^2B + \Sigma XA$

From (2) since $\Sigma A = NA$ where (4) $\Sigma Y = \Sigma XB + NA$

N = number of observations

Multiply (3) by $\frac{1}{\Sigma X}$ (5) $\frac{\Sigma XY}{\Sigma X} = \frac{\Sigma X^2B}{\Sigma X} + A$

Multiply (4) by $\frac{1}{N}$ (6) $\frac{\Sigma Y}{N} = \frac{\Sigma XB}{N} + A$

Subtracting to solve for B. $\frac{\Sigma XY}{\Sigma X} - \frac{\Sigma Y}{N} = \frac{\Sigma X^2B}{\Sigma X} + A - \frac{\Sigma XB}{N} - A$

$$\frac{\Sigma XY}{\Sigma X} - \frac{\Sigma Y}{N} = B\left[\frac{\Sigma X^2}{\Sigma X} - \frac{\Sigma X}{N}\right]$$

$$B = \frac{\frac{\Sigma XY}{\Sigma X} - \frac{\Sigma Y}{N}}{\frac{\Sigma X^2}{\Sigma X} - \frac{\Sigma X}{N}}$$

From (6) $A = \frac{\Sigma Y}{N} - \frac{\Sigma XB}{N}$

their respective straight line trends. For the purpose of comparison the fitted trends of the data for females and males are depicted in figure 25. The trends for both sexes practically coincide, demonstrating no essential sex differences in the size of the head. For this reason, most of the comparisons of maldeveloped cases with the normal have been made without regard to sex.

DIVISION OF DATA

The data for normal and abnormal material have each been divided according to sex for further comparisons in the study of certain dimensions of the palate, namely, the widest transverse diameter of the

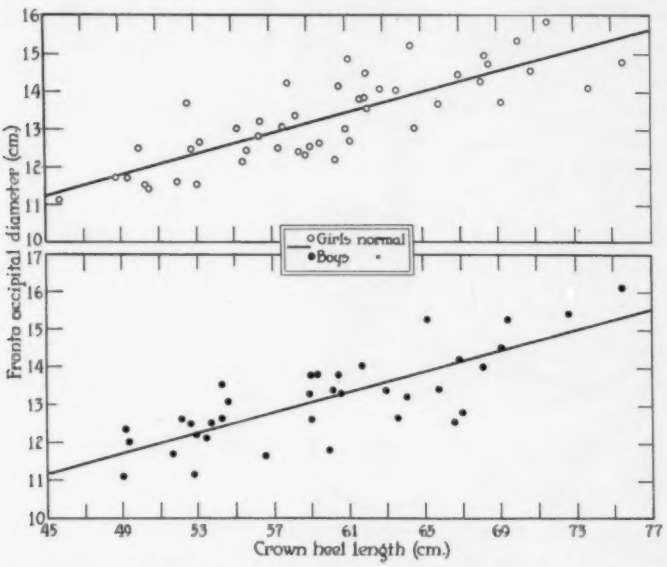

Fig. 11.—Field graphs and trend of the fronto-occipital diameter with body length of the female and male children of this study.

palate, actual surface width of the palate and height of the palate. After these various divisions of the material were made, a straight line was fitted to the measurements of each group by the method of least squares. The root mean square or standard deviation, probable error, and the probable error of the trend were computed for each group.[3] The result of these computations are recorded in table 9.

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3. Standard deviation: $\sigma = \sqrt{\frac{\Sigma\Delta^2}{N}}$

Probable error: $P.E. = 0.6745\sigma$

Bowley: Elements of Statistics, ed. 4, London, P. S. King & Son, 1920, p. 270.

Probable error of the trend: $P.E.T. = \frac{P.E.}{\sqrt{N}}$

Kelley: Statistical Method, New York, The Macmillan Company, 1923, p. 105.

TABLE 9.—*Table of Formulas*

Dimension	Data Included	Number of Observations	Formula	Root Mean Square Deviation, Cm.	P. E.	P. E.m	Average Deviation	Average per Cent Deviation
Fronto-occipital diameter	Combined male, female (normal)	86	$y = 5.067 + 0.136\ L$	0.677	0.457	0.049	0.553	4.06
	Combined male, female (maldeveloped)	27	$y = 5.495 + 0.129\ L$	0.641	0.432	0.083	0.537	4.50
	Male (normal)	38	$y = 4.958 + 0.137\ L$	0.692	0.467	0.075	0.565	3.64
	Female (normal)	48	$y = 5.106 + 0.136\ L$	0.662	0.447	0.065	0.550	4.12
Widest transverse diameter of palate	Combined male, female (normal)	91	$y = 2.025 + 0.022\ L$	0.181	0.122	0.013	0.148	4.48
	Combined male, female (maldeveloped	28	$y = 3.799 - 0.0001\ L$	0.260	0.168	0.032	0.214	5.64
	Male (normal)	40	$y = 2.216 + 0.020\ L$	0.146	0.098	0.016	0.117	3.43
	Female (normal)	51	$y = 1.787 + 0.025\ L$	0.183	0.123	0.017	0.142	4.33
	Male (maldeveloped)	22	$y = 4.100 - 0.005\ L$	0.263	0.177	0.038	0.210	5.50
	Female (maldeveloped)	6	$y = 1.857 + 0.031\ L$	0.197	0.128	0.052	0.148	3.94
Actual surface width of palate	Combined male, female (normal)	91	$y = 2.181 + 0.030\ L$	0.205	0.138	0.015	0.165	4.17
	Combined male, female (maldeveloped)	28	$y = 1.905 + 0.033\ L$	0.282	0.190	0.036	0.218	5.85
	Male (normal)	40	$y = 2.483 + 0.026\ L$	0.197	0.133	0.021	0.166	4.12
	Female (normal)	51	$y = 1.829 + 0.035\ L$	0.193	0.130	0.018	0.150	3.84
	Male (maldeveloped)	22	$y = 2.157 + 0.028\ L$	0.320	0.216	0.046	0.250	6.76
	Female (maldeveloped)	6	$y = 2.116 + 0.031\ L$	0.067	0.045	0.018	0.053	1.34
Height of palate	Combined male, female (normal)	91	$y = 0.570 + 0.006\ L$	0.101	0.068	0.007	0.079	1.44
	Combined male, female (maldeveloped)	28	$y = 1.221 - 0.0002\ L$	0.100	0.068	0.013	0.073	6.02
	Male (normal)	40	$y = 0.672 + 0.004\ L$	0.105	0.071	0.011	0.085	0.93
	Female (normal)	51	$y = 0.403 + 0.009\ L$	0.093	0.063	0.009	0.073	7.55
	Male (maldeveloped)	22	$y = 1.176 + 0.0007\ L$	0.114	0.077	0.016	0.083	6.80
	Female (maldeveloped)	6	$y = 1.310 - 0.002\ L$	0.068	0.046	0.019	0.053	4.49
Length of alveolar process	Combined male, female (normal)	91	$y = 2.015 + 0.019\ L$	0.179	0.121	0.013	0.145	4.61
	Combined male, female (maldeveloped)	28	$y = 1.824 + 0.023\ L$	0.176	0.114	0.022	0.135	4.36
Width of cleft	Combined male, female	27	$y = 2.622 - 0.018\ L$	0.222	0.150	0.029	0.177	13.80

ANALYSIS OF THE DIFFERENCE BETWEEN NORMAL AND CLEFT PALATES

The measurements of the normal child and the abnormal child were graphically compared. The method was similar for each set of dimensions. A field graph of the palate measurements of the normal children with body length is presented with their fitted trend and three times its probable error. Field graphs of the measurements of the abnormal children with body length is also presented with their fitted trend and three times its probable error. For purposes of comparison, the fitted trends of the normal and abnormal children are depicted in figure 25 in their actual relation to each other.

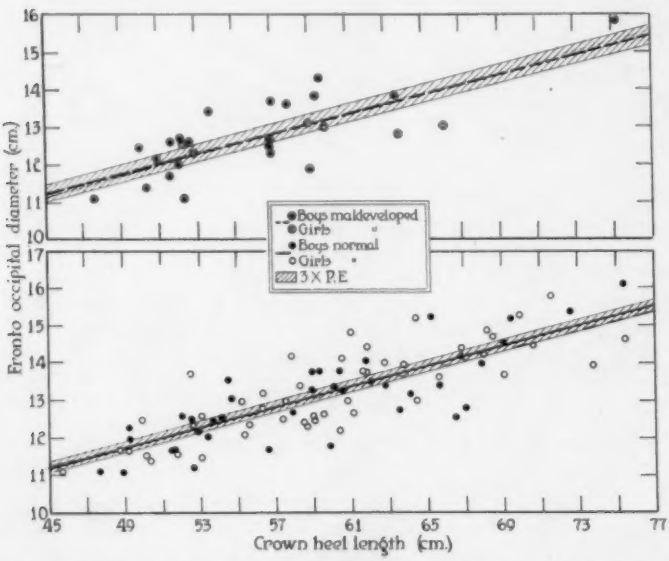

Fig. 12.—Field graphs of the fronto-occipital diameter with body length for the abnormal children and for the normal children. The fitted trend and three times the probable error is indicated in each graph.

Fronto-Occipital Diameter.—The fronto-occipital diameter of the normal children is compared with the same dimensions of the maldeveloped children in figure 12. A field graph of the fronto-occipital diameter of the normal children with body length is presented with their fitted trend and three times its probable error. A field graph of the fronto-occipital diameter of the abnormal children with body length is also presented with its fitted trend (indicated in broken line) and three times its probable error. For the purpose of comparison, the fitted trends of the normal and abnormal children are depicted in

figure 25. It is evident that there is no significant difference in the fronto-occipital diameter in these two groups, their trend falling well within the range of three times the probable error. The size of the head is therefore approximately the same for the normal, as for the maldeveloped material.

Surface Width of the Palate.—The surface width of the normal palate is compared with that of the cleft palate in figure 13. Field graphs of both the normal and maldeveloped children are depicted. The range of three times the probable error of the trend is indicated in each field graph. For the purpose of comparison, the lines of trend for both groups of data are depicted in figure 25. Growth is definitely indicated, but it is doubtful if there is a significant difference in the surface width of the palate in the normal and maldeveloped children. An increment is demonstrated of approximately 8 mm. in the surface

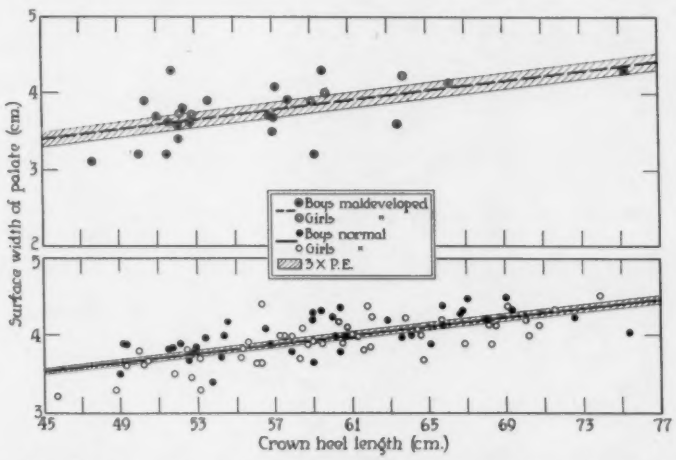

Fig. 13.—Field graphs of the surface width of the palate with body length for the abnormal children and the normal children. The fitted trend and three times the probable error is indicated in each graph.

width of the normal palate during that portion of the growth period included in this study, and a very similar amount of growth in the cleft palate. The fitted line of trend for the maldeveloped material for 51 cm. length is approximately 1.3 mm. less than that for the normal material and at 59 cm. length it is 1 mm. less. The foregoing points, 51 and 59 cm., are chosen because the majority of the maldeveloped material is included within this length. This apparent difference in surface width is probably not significant. It may be due to greater difficulty in getting the end-point of measurement at the medial edge

of the cleft palate, or it may be the result of chance selection in the small group of the maldeveloped children. That chance selection is a cause for this difference is supported by analysis of the same data when divided according to sex. Field graphs of the data for males and

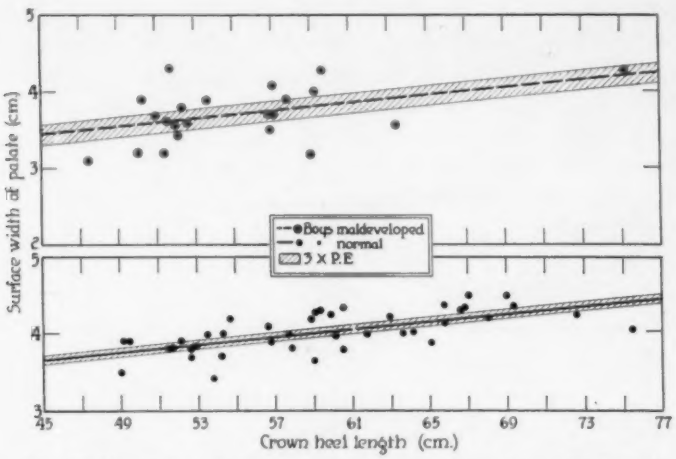

Fig. 14.—Field graphs of the surface width of the palate with body length for the abnormal and normal boys of this series. The fitted trend and three times the probable error is indicated in each graph.

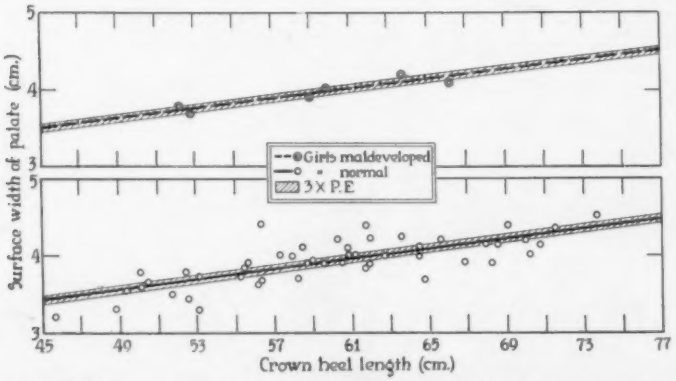

Fig. 15.—Field graphs of the surface width of the palate with body length for the abnormal and normal girls of this series. The fitted trend for each group of data and three times the probable error is indicated in each graph.

females are depicted in figures 14 and 15, respectively. Their lines of trend and the range of three times the probable error are indicated. For the purpose of comparison, the line of trend of each group of normal

data is depicted in figure 25 in its actual relation to the fitted trend of the abnormal material of the same sex. The fitted trend of the abnormal male children at 51 cm. length is approximately 2.5 mm. below that of the normal male children and at 59 cm. length it is approximately 2 mm. below that of the normal children, while on the other hand, the fitted trend of the maldeveloped females indicates a wider actual surface width in the cleft than in the normal palate.

Widest Transverse Diameter of the Palate.—The widest transverse diameter of the palate is depicted in figure 16, in which field graphs of the normal children and the maldeveloped children are presented with the trend for each group of data. Three times the probable error of the

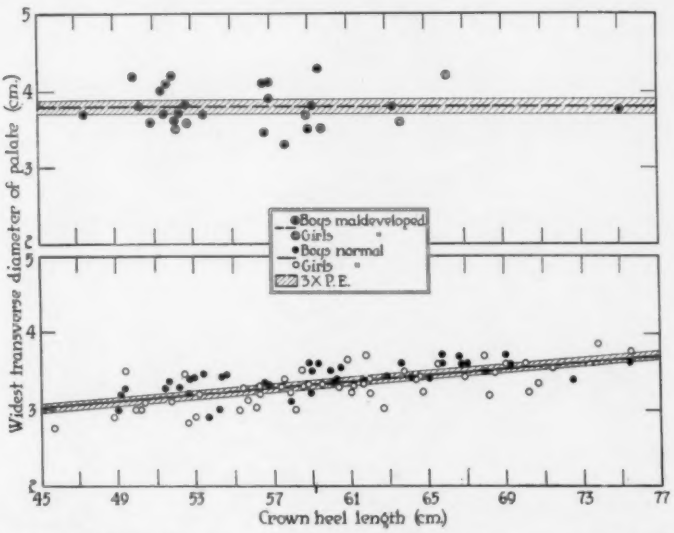

Fig. 16.—Field graphs of the widest transverse diameter of the palate with body length for the abnormal and normal children of this series. The fitted trend and three times the probable error is indicated in each graph.

fitted trend is indicated in each field graph. For the purpose of comparison, the fitted trend of each group of data is depicted in figure 25. Definite growth and also significant difference in the widest transverse diameter between the normal and the cleft palate is indicated. Approximately 6 mm. increase in width of the normal palate during the period of growth included in this study is demonstrated but no increase in the width of the cleft palate. Since the fitted line of trend for the cleft palate shows no spread or increase of the width of the maxillae during the period included in this study, therefore, if this material is representative, any growth which does occur is toward the midline. This would

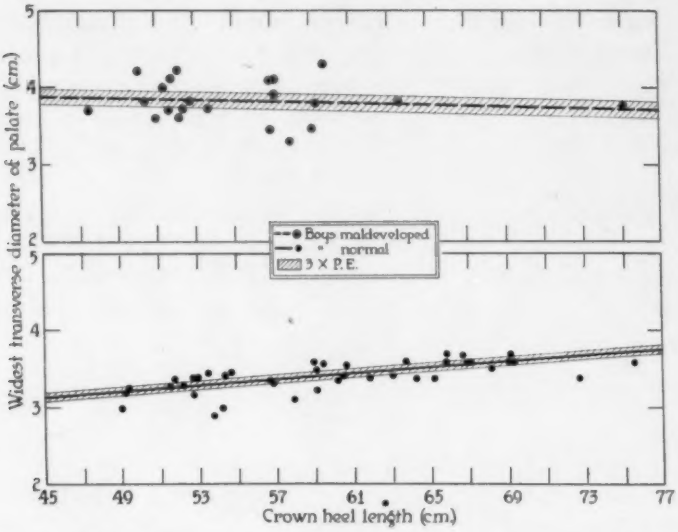

Fig. 17.—Field graphs of the widest transverse diameter of the palate with body length for the abnormal and normal male children. The fitted trend and three times the probable error is indicated.

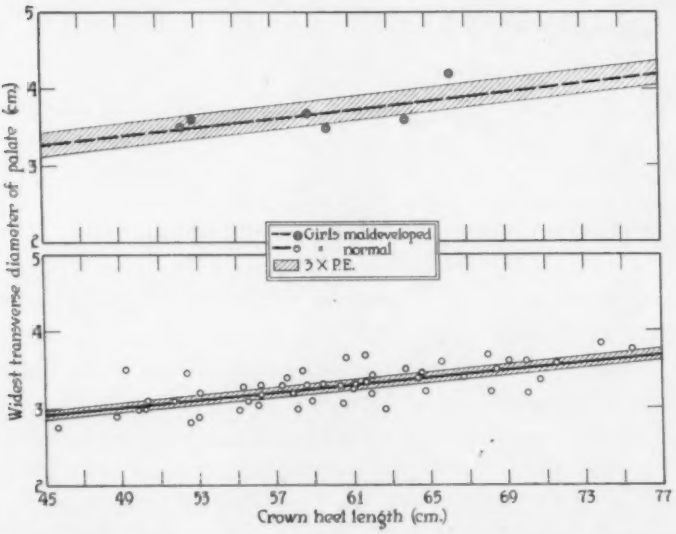

Fig. 18.—Field graphs of the widest transverse diameter of the palate with body length for the abnormal and normal female children. The fitted trend and three times the probable error is indicated in each graph.

lead one to expect that the cleft would become narrower as growth occurred in the palate. To check this, the width of the cleft was measured, and analysis of these measurements confirmed this supposition (fig. 23). This is the most unexpected and remarkable observation demonstrated in this study. That the transverse diameter of the cleft palate is greater than the transverse diameter of the palate of the normal child of equal body length is evident. The difference in width at the 51 and 59 cm. lengths is approximately 7 and 5 mm., respectively. With the data grouped according to sex, field graphs and their trend for measures of the widest transverse diameter of the cleft and normal palate are depicted in figures 17 and 18 for male and female children respectively. For the purpose of comparison, the line of trend for the measures of male children, normal and abnormal, are depicted in

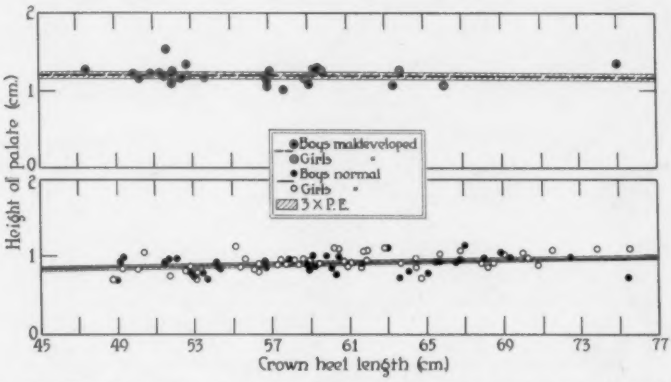

Fig. 19.—Field graphs of the height of the palate with body length for the abnormal and normal children of this series. The fitted trend and three times the probable error is indicated in each graph.

figure 25 in their actual relation to each other, and the lines of trend for the measures of the female children are also depicted in similar manner in figure 25. As a whole, the results are similar to those in which no division as to sex was made.

Height of Palate.—Comparison of the height of the palate is depicted in figure 19, which is composed of field graphs and their trends for the measures of normal children and the maldeveloped children. Three times the probable error of the trends is indicated in each field graph. For the purpose of comparison, the trends of each group is depicted in figure 25. There is little increase in height during the period studied, approximately 1 mm. for the normal palate and no increase for the cleft palate. That the cleft palate is definitely higher than the normal palate of children of the same body length, is demonstrated. At 51 cm. crown-

heel length, the trend for the maldeveloped material is approximately 3 mm. higher and at 59 cm. length 2.5 mm. higher. With the data grouped according to sex, field graphs and their trend for measures of the height of the normal palate and the cleft palate are depicted in figures 20 and 21 for the males and females, respectively. Three times

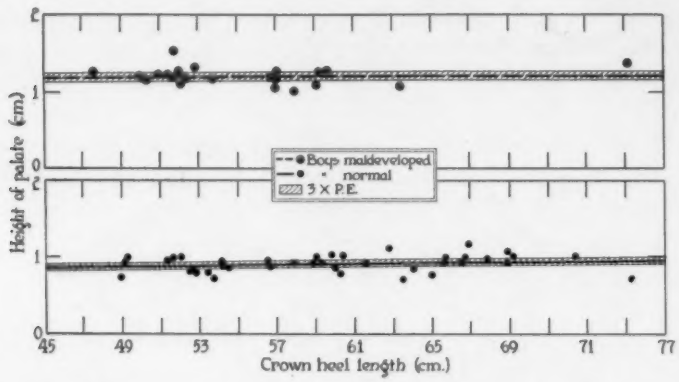

Fig. 20.—Field graphs of the height of the palate with body length for the abnormal and normal male children. The fitted trend and three times the probable error is indicated in each graph.

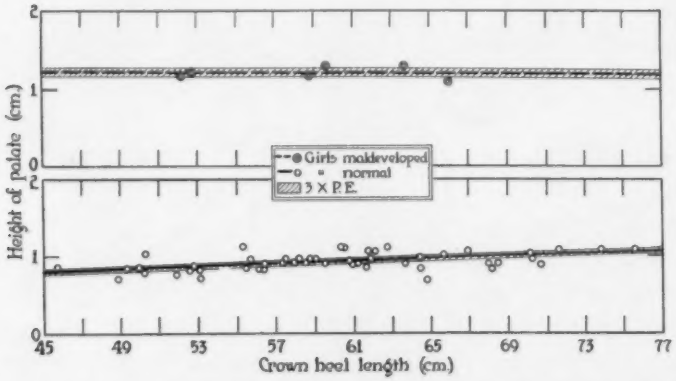

Fig. 21.—Field graphs of the height of the palate with body length for the abnormal and normal female children. The fitted trend and three times the probable error is indicated in each graph.

the probable error of the fitted trends for each group is depicted. For the purpose of comparison, the lines of trend for measures of the male children, normal and abnormal, are depicted in figure 25 in their actual relation to each other, and the lines of trend for measures of the female

children are also depicted in similar manner in figure 25. In general, the result is similar to that for the combined data.

Length of the Alveolar Process.—The values determined for length of the alveolar process in the maldeveloped children were divided into three groups: the long side, the short side and the average of both sides in a case of bilateral cleft. There were twenty in each of the first two groups and eight in the latter. The arithmetical mean of each of these groups of dimensions was taken. For the long side it was 3.05 cm.; for the short side, 3.11 cm., and 3.08 cm. for the average length of the bilateral cleft palates. This reveals a discrepancy of less than 1 mm., which is within the possible error of measurement.

The length of the alveolar process of the palate is depicted in figure 22, which consists of field graphs and their line of trend for the

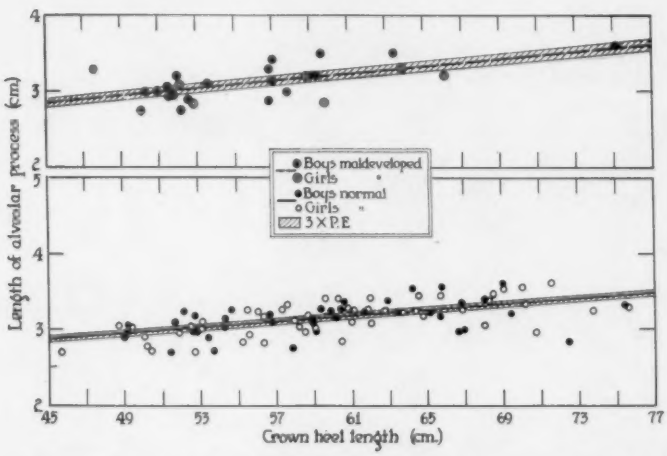

Fig. 22.—Field graphs of the length of the alveolar process with body length for the abnormal and normal children. The fitted trend and three times the probable error is indicated in each graph.

measures of the normal children and the maldeveloped children. Three times the probable error of the fitted trends is indicated in each field graph. For the purpose of comparison, the lines of trend of each group of data is depicted in figure 25.

Growth in length of the alveolar arc of the normal palate is approximately 5 mm. during the period included in these data, and as much, if not slightly more, in the alveolar arc of the cleft palate.

Although, on the whole, in the maldeveloped children the fitted trend for length of the alveolar process with body length is slightly above that of normal children, it does not appear to be a significant difference. In that portion of the graph which includes most of the

maldeveloped material, namely, from 51 to 59 cm. crown-heel length, it is not greater than 0.5 mm. It is possible that some of this difference in length is due to the difference in the method of obtaining these dimensions. The normal palate was measured directly as the chord of the arc of one side of the alveolar process. The maldeveloped palate was measured for the most part as two segments or chords, the sum of whose circumference represented the entire alveolar arc, that is, the arc of the maxillary portion of the alveolar border and one-half the premaxilla were summated to obtain the length of the alveolar arc. Since the sum of two chords is greater than the chord of the sum of the circumference they represent, this probably is a slight source of error in the direction indicated by the lines of trend.

Width of the Cleft.—Since analysis of the widest transverse diameter of the palate demonstrated an increase of approximately

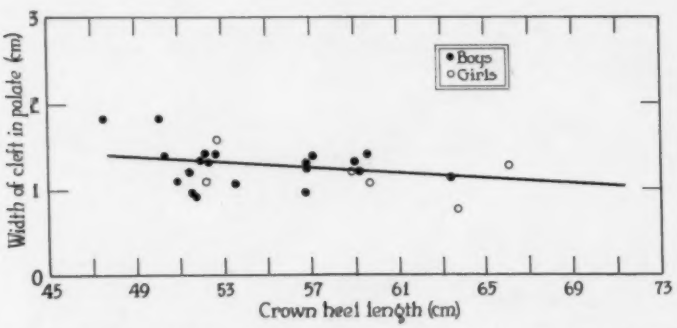

Fig. 23.—A field graph of the width of the cleft with body length. The fitted trend is indicated.

7 mm. in the first year and no increase in the same dimension of the cleft palate during this same period, although there was growth in the palate of both the normal and abnormal children, as demonstrated by the actual surface measurement, it should follow that the cleft becomes smaller or more narrow during the period of growth included in this investigation. This supposition is supported by analysis of measures of the cleft. A field graph of the width of the cleft and its line of trend is depicted in figure 23. Between the extreme ends of the graph it diminishes approximately 4 mm. The material is so variable that this may be a chance selection of wide clefts in the smaller specimens, but since it checks so well with the other observations it is more probable that there is actual growth of the tissues toward the midline. This can be checked by repeated measurements on the same child over a period of several months.

COMMENT

Comparison of the results of this investigation with the dimensions of the palate, as determined by other investigators, cannot be accurately made, since their results have not been analyzed in this manner, the age distribution of material does not correspond, and the method of taking and the end-points of measurements are not the same. In general, however, there is a similarity of results. In table 10 are recorded the results of investigators quoted in the section on literature and included are those of this investigation for comparison.

Congenital malformations of the upper lip and palates are most common in boys. Haug reported that in 2,352 instances of such maldevelopment the male was effected in 64.3 per cent. Davis reported 24 children with clefts, 71 per cent of whom were boys. In this series there were 20 boys and 6 girls, or 77 per cent males and 23 per cent females.

TABLE 10.—*Dimensions of the Palate Compared with Results of Other Investigators*

Investigator	Dimension		
	Width, Cm.	Height, Cm.	Length, Cm.
Alkan (average)	2.70	1.20	3.20
Denzer (average)	3.09	0.88	....
Franke (average)	....	....	2.68
This study (median)	3.30	0.95	3.15

Congenital clefts of the upper lip and upper part of the face are most common on the left side. Haug reported 2,238 cases with left-sided cleft in 50.9 per cent, right-sided in 21.8 per cent and bilateral in 27.3 per cent. In general, only complete clefts are included in the series of this investigation and are not entirely comparable, therefore, with this report of Haug where all clefts were included. This may be the reason in part for the difference in frequency in this series, namely, left-sided cleft, 38 per cent; right-sided cleft, 35 per cent and bilateral cleft, 27 per cent.

The results of this investigation would, of course, have been more conclusive if the maldeveloped material was represented by a larger series. Anomalies of the upper part of the face and jaw are not of frequent occurrence. They occur in colored people once in 1,788 births and in white people once in 915 births, according to the figures of Davis who reviewed the birth records of 28,085 consecutive deliveries in which there occurred 24 instances of cleft. Frobelius, in 1865, reported 76 instances of cleft in 180,000 hospital admissions, or approximately

1 to every 2,400. Since complete clefts, unilateral or bilateral, were chosen for the present study, many cases with lesser degrees of cleft were rejected. Complete clefts, unilateral or bilateral, occurred in 73.4 per cent of 1,887 cases of clefts of the lip and palate reported by Haug, 24 per cent of which were complete bilateral clefts of the lip, process and palate.

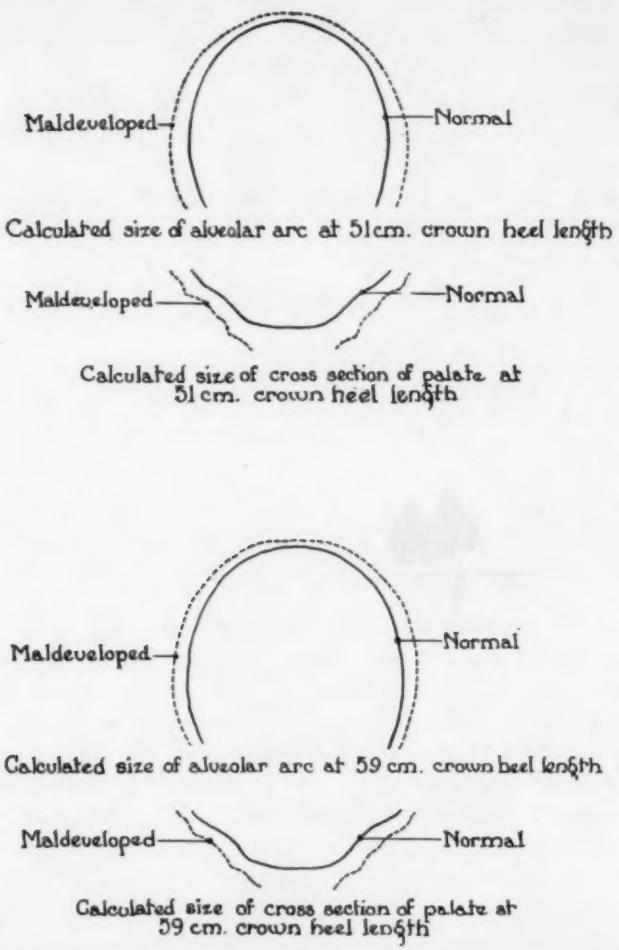
Maldeveloped
Normal
Calculated size of alveolar arc at 51 cm. crown heel length
Maldeveloped
Normal
Calculated size of cross section of palate at 51 cm. crown heel length
Maldeveloped
Normal
Calculated size of alveolar arc at 59 cm. crown heel length
Maldeveloped
Normal
Calculated size of cross section of palate at 59 cm. crown heel length

Fig. 24.—An outline of the alveolar process and a cross-section of the palate depicting, as determined in this study, the relative size of the abnormal and normal palate at 51 cm. crown-heel length and 59 cm. crown-heel length.

Other problems in connection with surgical measures on maldevelopments of the upper lip and palate could be solved by this method, especially should the anatomic results of operations be investigated.

SUMMARY

Growth increments of the normal palate during approximately the first year (from 49 to 75 cm. crown-heel length) are as follows:

Widest transverse diameter of palate	5.5 mm.
Actual surface width of palate	8.0 mm.
Height of palate	1.0 mm.
Length of alveolar process	5.0 mm.

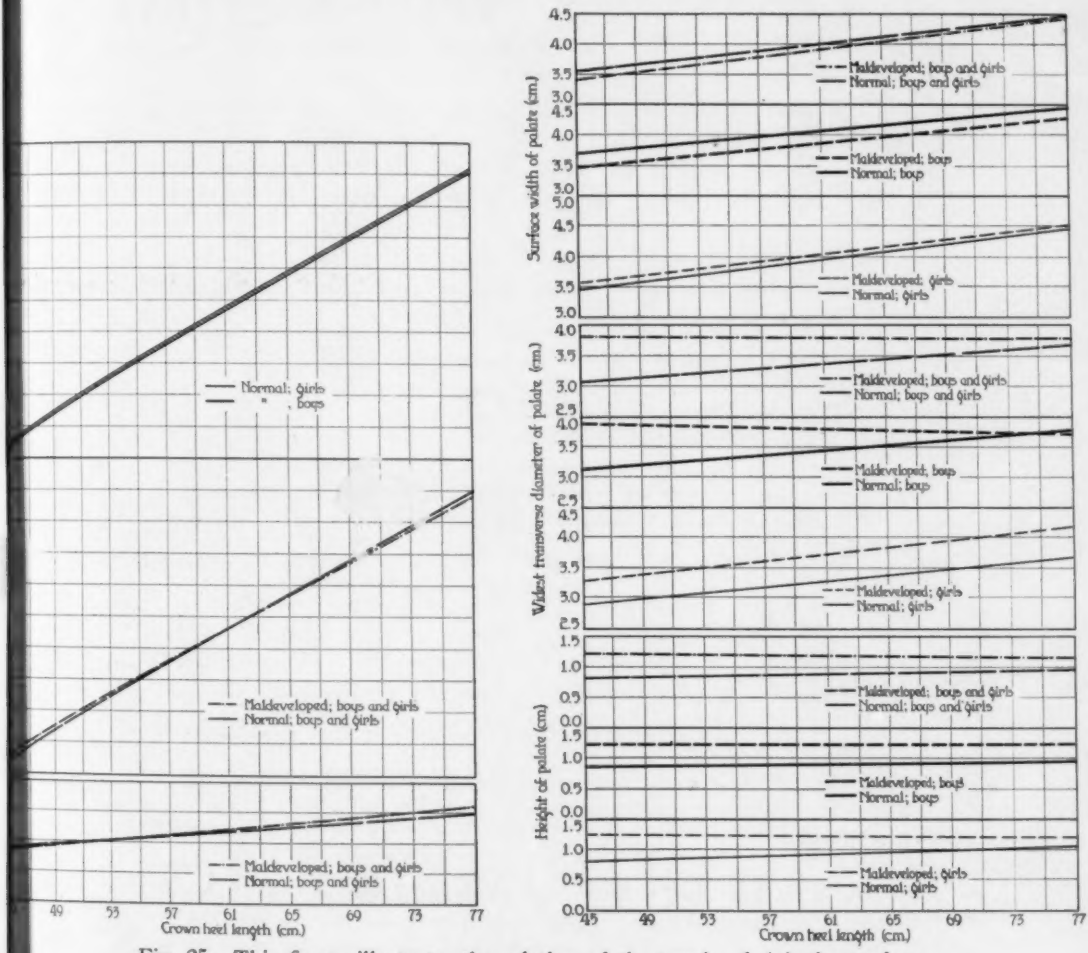

Fig. 25.—This figure illustrates the relation of the trends of (*a*) the surface width of the palate with body length, (*b*) the widest transverse diameter of the palate with body length, (*c*) the height of the palate with body length, (*d*) the fronto-occipital diameter of the head with body length, and (*e*) the length of the alveolar process of the palate with body length.

Dimensions of cleft palate, except surface width, are larger than those of the normal palate. The cleft palate dimensions compared with those

of the normal palate for children of 51 and 59 cm. crown-heel length, respectively, are as follows:

	51 cm. crown-heel length, mm.	59 cm. crown-heel length, mm.
Widest transverse diameter of palate.....	+7.0	+5.0
Actual surface width of palate.....	—1.3	—1.0
Height of palate	+3.0	+2.5
Length of alveolar process.....	0.0	+0.5

These differences in the size of the cleft palate and the normal palate are graphically represented in figure 24.

The width of the cleft was found to diminish 1.5 mm. during the growth interval between 51 and 59 cm. crown-heel length. This was to be expected, after it was found that the widest transverse diameter during the same interval remained approximately unchanged.

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HISTOLOGIC STUDIES OF THE BRAIN IN CASES OF FATAL INJURY TO THE HEAD

I. PRELIMINARY REPORT *

CARL W. RAND, M.D.
LOS ANGELES

Perhaps one of the most obvious gross changes found in the brain following a severe injury to the head is an increase in its fluid content. This is commonly referred to as cerebral edema. At autopsy the brain appears swollen, and under certain circumstances it is probably actually heavier than normal. The increase in fluid, as judged by gross appearance, is general in distribution. It is not confined to the substance of the brain alone, although this tissue may be wetter than normal; in addition, there is often an excess of fluid in the subarachnoid space and in the ventricular system. This excess of cerebrospinal fluid may be demonstrated clinically. At lumbar puncture the pressure of the fluid is usually increased, the rapidity of its flow is quickened, and the actual amount that may be withdrawn is often considerably greater than normal. The presence of a "wet" edematous brain is often seen at operation. The pathologic and physiologic changes underlying this increase in fluid content have not been sufficiently explained. The studies that will be briefly outlined in this report are being conducted for the purpose of investigating the sources of this fluid, as well as the reason for its increase.

The first inquiry was directed to a study of the choroid plexus. It seemed reasonable to assume that the activity of this structure might be altered by trauma. If so, this might lead to morphologic changes that could be seen under the microscope. Other considerations, however, soon presented themselves for investigation, and finally led to a histologic survey of more distant portions of the brain.

It was sought: to ascertain the condition of the ependymal lining of the ventricles and its possible rôle as an accessory source of cerebrospinal fluid; to study the changes that might occur in the neurons or glial cells proper; to examine the condition of the leptomeninges, in seeking an explanation of the so-called "wet or sweaty" brain; to investigate the condition of the substance of the brain, especially with reference to possible enlargement of the perivascular and pericellular spaces, and to attempt experimentally to determine whether fluid seeps through the semipermeable membranes of the small capillary walls into the perivascular and hence into the pericellular spaces.

* Submitted for publication, July 26, 1930.

Abundant material has been placed at our disposal through the kindness of Dr. A. F. Wagner of the coroner's department. We have chosen sixty-one pathologic brains for study, using ten normal brains as controls. Dr. Cyril B. Courville has been working on other phases of this study, and more detailed reports will be presented with him later.

HISTORICAL DATA

Weed [1] (1922) has given an excellent review of the generally accepted present conception of the sources and circulation of cerebrospinal fluid. The supposition that this fluid is secreted by the choroid plexuses is usually ascribed to Faivre [2] (1853) and Luschka [3] (1855). Faivre was the first to describe the glandular histologic structure of the choroid plexus. He demonstrated that the villous projections were covered by epithelial cells which he believed showed indications of secretory activity. Luschka originated the hypothesis "that the choroid plexuses elaborate the greater portion of the cerebrospinal fluid" and was the first to show hyalin-like inclusions in the cells. These may have been vacuoles. His hypothesis has been widely accepted, although conclusive proof that the choroid plexus is a secretory gland has never been actually established. Findlay [4] (1899) made the most careful study of the choroid plexus up to his time. He described the glandular structures of the cells and called attention to the pigmented globules and vacuoles in them. He concluded that "there is a constant change going on in the epithelial cells and they normally undergo a process of vacuolation and rupture to form the choroid plexus secretion." Studnicka [5] (1900) found similar evidence of secretion both in the cells of the choroid plexus and in the ependymal cells in certain areas. Pettit and Girard [6] (1902) described hyalin-like globules in the choroidal epithelium of animals, but thought that these did not represent secretory vacuoles. Loeper [7] (1904) studied the choroid plexus in man and described pigmented granules in the cells. He also found pigmented granules within the vacuoles by using osmic acid preparations, and concluded that the

1. Weed, L. H.: The Cerebrospinal Fluid, Physiol. Rev. **2**:171 (April) 1922.

2. Faivre, E.: Des granulationes meningiennes, Thèse de Paris, 1853.

3. Luschka, H.: Die Adergeflechte des menschlichen Gehirns, Berlin, 1855.

4. Findlay, J. W.: The Chorioid Plexuses of the Lateral Ventricles of the Brain: Their Histology Normal and Pathological, Brain **22**:161, 1899.

5. Studnicka, F. K.: Untersuchungen über den Bau des Ependyms der nervösen Centralorgane, Anat. Hefte **15**:303, 1900.

6. Pettit, A., and Girard, J.: Sur la fonction sécrétoire et la morphologie des plexus choroides des ventricles lateraux du systéme nerveux central, Arch. d'anat. micr. **5**:213, 1902.

7. Loeper, M.: Sur quelques points d'histologie normale et pathologique des plexus chorioides de l'homme, Compt. rend. Soc. de biol. **56**:1010, 1904.

choroid plexus was a glandular organ. From histochemical investigation Yoshimura [8] (1910) concluded that the secretion of cerebrospinal fluid by the choroid plexus "was related to the aggregation of the smaller cytoplasmic granules together into large vacuoles for discharge." Pellizzi [9] (1911) felt that the epithelial cells of the plexus secreted granules which increased in size by the absorption of fluid plasma until they were extruded.

More convincing evidence of this secretory nature of the choroid plexus has been established by physiologic and pharmacologic methods than by purely anatomic and histologic observations. Cappelletti [10] (1900) found that ether and pilocarpine increased the flow of spinal fluid, while atropine and hyoscyamine decreased it. Pettit and Girard [6] repeated his work, with similar observations. In addition, they made histologic studies of the choroid plexus and found an actual increase in the size of the choroidal epithelium. They described these cells as being practically doubled in height while under activity. They also noted a granular zone near the base of the cells and a clear, sometimes vesicular, zone near the apex, which they concluded indicated that the choroid plexus possessed a secretory activity. Meek [11] (1907) repeated their experiments, coming to identical conclusions, and stated that "the two things most striking about these modified cells are their great increase in height and the appearance of so much clear space at the distal side of the nucleus." Claisse and Levy [12] (1897) described hypertrophy of the choroid plexus in a case of internal hydrocephalus. Dandy and Blackfan [13] (1913) and Frazier and Peet [14] (1914) produced internal hydrocephalus experimentally by occlusion of the aqueduct of Sylvius. In 1919, Dandy [15] again produced unilateral hydrocephalus by obstructing one foramen of Monro in which the choroid plexus was left intact in

8. Yoshimura, K.: Das histochemische Verhalten des menschlichen Plexus chorioidens, Arb. a. d. neurol. Inst. a. d. Wien. Univ. **18**:1, 1910.

9. Peulizzi, B.: Experimentelle histologische untersuchungen über die Plexus chorioidei (Adergeflechte), Folia neuro-biol. **5**:305, 1911.

10. Cappelletti, L.: L'ecoulement de liquide cérebrospinal par la fistule céphalo-rachidienne en conditions normales et sous l'influence de quelques medicaments, Arch. ital. de biol. **35**:463, 1900.

11. Meek, W. J.: A Study of the Chorioid Plexus, J. Comp. Neurol. **17**:286, 1907.

12. Claisse, P., and Levy, C.: Etude histologique d'un cas d'hydrocéphalie interne, Bull. Soc. Anat. de Paris, 1897, p. 265.

13. Dandy, W. E., and Blackfan, K. D.: An Experimental and Clinical Study of Internal Hydrocephalus, J. A. M. A. **61**:2216 (Dec. 20) 1913.

14. Frazier, C. H., and Peet, M. M.: Factors of Influence in the Origin and Circulation of the Cerebrospinal Fluid, Am. J. Physiol. **35**:268, 1914.

15. Dandy, W. E.: Experimental Hydrocephalus, Ann. Surg. **70**:129 (Aug.) 1919.

the obstructed ventricle. When he removed the choroid plexus of the ventricle before obstructing the foramen of Monro, internal hydrocephalus did not occur. His experiments furnish the strongest evidence to prove that the choroid plexuses elaborate cerebrospinal fluid. Cushing [16] (1914), while operating on a child with a porencephalic cyst, observed exudation of a clear fluid from the surface of the choroid plexus. Becht [17] (1920), on the other hand, in a critical review not only questioned whether the choroid plexus secretes cerebrospinal fluid, but has also challenged the generally accepted theories of the circulation and absorption of this fluid as outlined by practically all other observers. However, he offered no adequate explanation as to the source or pathways of absorption of the fluid. Wislocki and Putnam [18] (1921) demonstrated that granules of potassium ferrocyanide penetrated the ependymal cells lining the ventricles, but did not pass through the choroidal epithelium, in cases of experimental internal hydrocephalus in which the solution was introduced into the subarachnoid spaces. Nañagas [19] (1921) demonstrated an increased intraventricular accumulation of fluid after intravenous injection of hypertonic salt solution, but in no case found apparent absorption of the fluid by the cells of the choroid plexus.

Weed [20] (1914), in discussing the dual source of cerebrospinal fluid, hypothecated that aside from the choroid plexus "the perivascular spaces also pour a certain amount of fluid into the subarachnoid space, where this fluid mixes with the liquid produced in the cerebral ventricles." He failed to tell how the fluid gets into the perivascular spaces. He was of the opinion that "the ependymal cells lining the cerebral ventricles and central canal of the spinal cord may also contribute even in the adult a minimal addition to the intraventricular cerebrospinal fluid." Halliburton [21] (1916) referred to the cerebrospinal fluid as serving as the lymph of the brain, although he differentiated it from the true lymph as seen in lymphatic vessels. It is generally conceded that true lymphatic vessels do not exist in the dura mater or the brain. Sabin [22] (1915-1916) pointed out that the use of the term "lymph" should be restricted to the fluid confined to true lymphatic vessels and should not be used to desig-

16. Cushing, H.: Studies on Cerebro-Spinal Fluid, J. M. Research **31**:1, 1914.

17. Becht, F. C.: Studies on Cerebrospinal Fluid, Am. J. Physiol. **51**:1, 1920.

18. Wislocki, G. B., and Putnam, T. J.: Absorption from Ventricles in Experimentally Produced Internal Hydrocephalus, Am. J. Anat. **29**:313, 1921.

19. Nañagas, J. C.: Experimental Studies on Hydrocephalus, Bull. Johns Hopkins Hosp. **32**:381, 1921.

20. Weed, L. H.: Studies on Cerebrospinal Fluid: IV. The Dual Source of Cerebrospinal Fluid, J. M. Research **31**:93, 1914.

21. Halliburton, W. D.: The Possible Functions of Cerebrospinal Fluid, Lancet **2**:779 (Nov. 4) 1916.

22. Sabin, F. R.: The Method of Growth of the Lymphatic System, Harvey Lectures, series 11, New York, 1915-1916.

nate any other fluid in the body. Weed [1] summarized the relationship of cerebrospinal fluid to the brain proper as follows:

> In one respect the cerebrospinal fluid does function as an accessory fluid to the central nervous system. . . . The drainage of the fluid contained within the perivascular channels toward the subarachnoid space has been commented upon; this fluid really becomes added to the ventricular cerebrospinal fluid in the subarachnoid spaces. . . . In that sense, then, these perivascular spaces represent accessory drainage channels, uninterrupted by cell membranes and capable of carrying toward the subarachnoid space the waste products of nerve-cell activity. Lacking a true lymphatic system, the nervous tissue apparently makes use of these perivascular channels as pathways for fluid elimination. The ultimate connection of these perivascular channels with potential spaces about each nerve-cell indicates the close relationship between the cerebrospinal fluid and the nervous system. And in addition to these rather obvious fluid spaces about the nerve-cells, there is evidence indicating that this fluid-system is intimately connected with the general tissue-channels through the ground-substance of the brain. The general direction of flow of this fluid under normal conditions seems to be toward the subarachnoid space. But under certain conditions this direction of flow may be reversed so that the cerebrospinal fluid passes from subarachnoid space to nerve cell (page 119).

CHANGES IN THE CHOROID PLEXUS

The choroid plexus is derived from a tufting of the ependymal lining of the ventricles. Each tuft is covered by a single layer of cuboidal epithelial cells which rest on a basement or limiting membrane (figs. 1 and 2). The fibrous tissue of the stroma is minimal, and the basement membrane usually approximates the wall of a central blood vessel. Definite changes in the choroid plexus have been noted in cases of fatal injury to the head. The most striking alteration is seen in the connective tissue of the stroma in which varying degrees of edema occur. In some instances there is but little distention of the connective tissue, in others diffuse swelling of the cells has occurred (fig. 3). In the most marked instances the villus is ballooned out with fluid so that the basement membrane is separated to the greatest extent from the underlying blood vessel (fig. 4). The fluid causing this edema may be seen to collect in large spaces between the walls of the blood vessels and the basement membrane of the choroidal epithelium (fig. 5). In some instances the accumulations of fluid are small and numerous, simulating bubbles; in others they may be large and cause a breaking down of the intervening septums. The blood vessels may be enlarged and distended, indicating hyperemic changes. The connective tissue cells may show swelling of the nucleus so that it appears vesicular and more round or oval than usual. These cells may take bizarre shapes and may be vacuolated. Pigmentation in the form of small granules is often present in the epithelium and stroma. The pigmented granules are usually contained in phagocytic cells. This pigmentation has been described by Flather [23] as

23. Flather, M. D.: A Study of the Haemosiderin Content of the Choroid Plexus, Am. J. Anat. **32**:125 (Sept.) 1923.

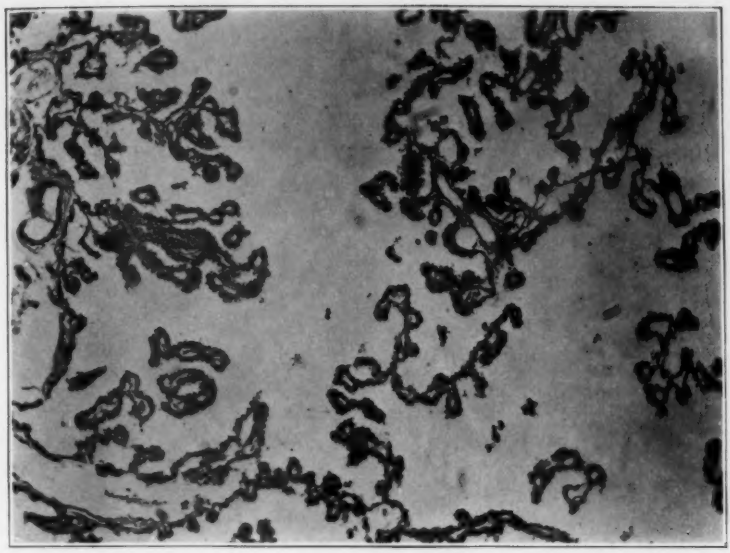

Fig. 1.—Normal choroid plexus. Various tufts of choroid plexus are seen. These are covered by a single layer of epithelium. The basement membrane on opposite sides of each villus is practically in coaptation, except where it is forced apart by the vessel. The stroma is inconspicuous, except near the pedicle of the gland. Hematoxylin and eosin stain; × 180.

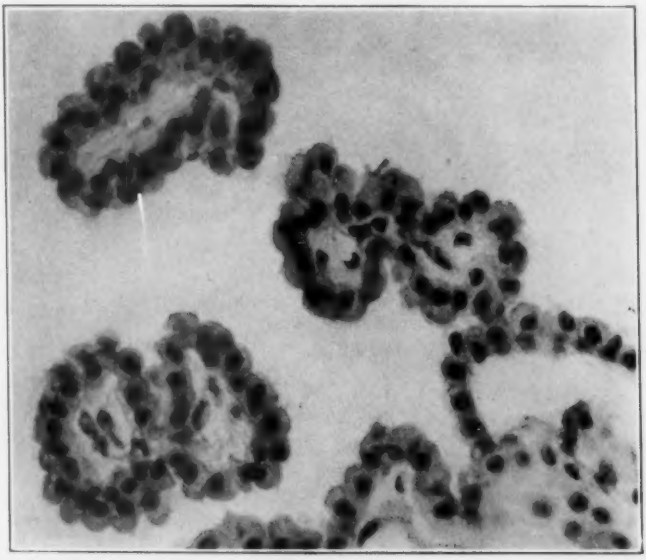

Fig. 2.—Normal choroid plexus. Tufts of normal choroid, showing the proximity of the wall of the central artery to the basement membrane of the choroidal epithelium. A few small vacuoles can be seen in the epithelial cells. Hematoxylin and eosin stain; × 550.

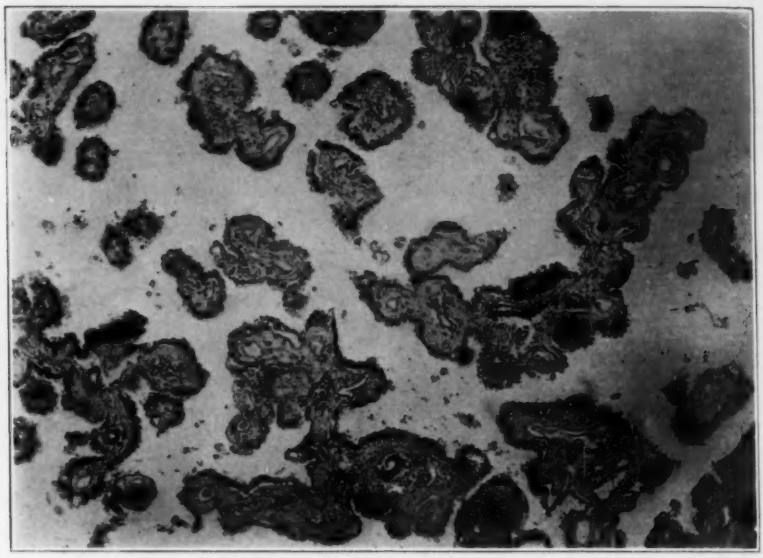

Fig. 3.—Moderate edema of the choroid plexus. The connective tissue of the stroma is moderately filled with fluid, forcing apart the choroidal epithelium. The spaces between the blood vessels and the choroidal epithelium are also widened. "Fibrin thrombi" are conspicuous. Those are not considered pathologic, as they are often seen in normal cases. Death occurred two hours after injury. Hematoxylin and eosin stain; × 190.

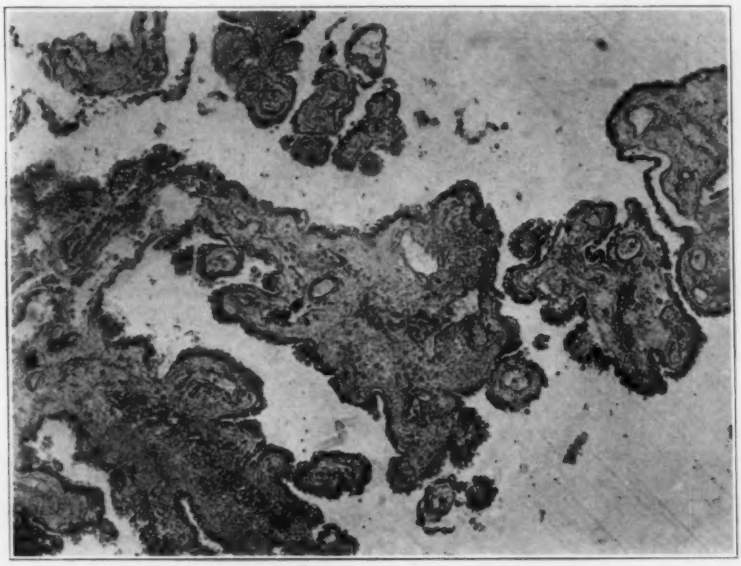

Fig. 4.—Marked edema of the choroid plexus. The stroma is expanded to the fullest extent by fluid. The choroidal epithelium is forced far apart, and the distance between the blood vessels and the basement membrane is greatly widened. Areas of pigment may be seen. This represents maximum edema of the choroid seen in this series. Death occurred four hours after injury. Hematoxylin and eosin stain; × 190.

hemosiderin, but it appears to be noniron pigment, possibly hematoidin, as demonstrated by the specific reaction to the test with potassium ferrocyanide. Masses of "fibrin thrombi" are sometimes found in normal, as well as in pathologic, cases, which contain iron pigment as demonstrated by the same test. They usually increase in numbers as age advances.

The basement membrane is found to be intact when the accumulation of fluid within the connective tissue is small. When the edema is more extensive, free fluid is found in large spaces in the stroma and the basement membrane is often torn. In certain instances it is distorted, or even totally destroyed, so that the inferior aspect of the epithelial cells is extensively irregular and it appears as if fluid were being forced

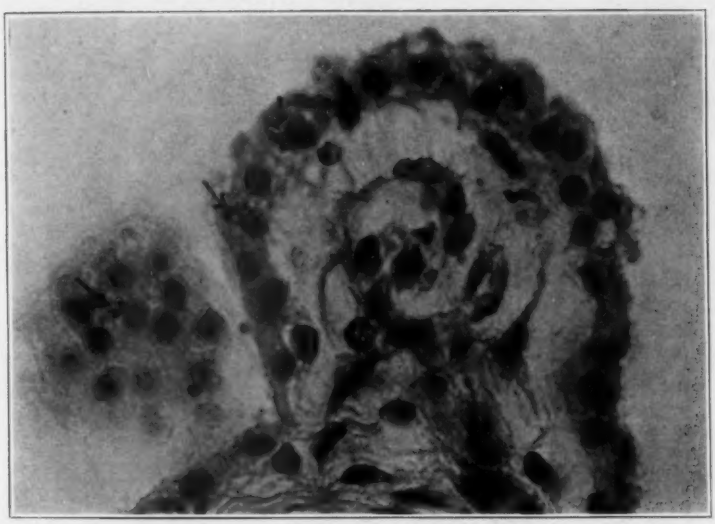

Fig. 5.—Enlarged collections of fluid in the choroid plexus following injury. A marked increase in the fluid spaces between the blood vessels and the basement membrane of the choroidal epithelium is seen. There is a definite increase in the vacuolization of the cells. A vacuole in the process of rupturing is seen at the top. In several locations pigment granules, indicated by arrows, may be seen. Death occurred two days after injury. Hematoxylin and eosin stain; × 850.

between them. The individual choroidal epithelial cells were often swollen and enlarged. In comparison to choroidal epithelial cells of normal height, i. e., 12 microns, cells varying from 14 to 20 microns in height are found, depending on the degree of edema. In certain instances cells measuring as high as 26 microns have been encountered. Often the free or ventricular margin of the cell is ragged, probably owing to its rupture by the passage through it of the contents of one large or many small vacuoles as they empty into the ventricle.

Vacuolization of the choroidal epithelium is normally seen in approximately from 12 to 20 per cent of the cells. The vacuoles may be multiple, in which case they are seldom large. Following trauma, vacuolization is greatly increased and may involve from 25 to 67 per cent of the cells. The vacuoles are often much larger than one sees in normal choroidal epithelium. Single vacuoles actually larger than a normal epithelial cell have frequently been observed (fig. 6). The process of the formation of these vacuoles is not clear. Some have thought that they result from a coalescence of granules in the cells. From our study it would appear

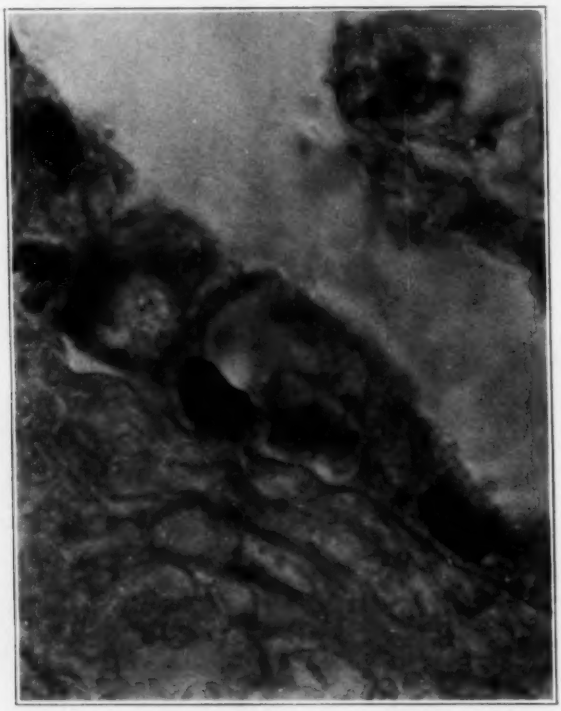

Fig. 6.—Large vacuole of choroid plexus about to rupture into the ventricle. There are many fine vacuoles scattered throughout the epithelial cells. To the left of the large central vacuole, which points toward the free margin, one sees a collection of minute vacuoles apparently coalescing to form a large one. Marked edema of the stroma and a moderate irregularity of the basement membrane are seen. The choroidal epithelium is markedly distorted. Death occurred four hours after injury. Hematoxylin and eosin stain; × 1,800.

that in certain instances fluid pushes up through the basement membrane of the cells, actually causing the formation of vacuoles within that structure. Some observers have described various inclusions of cells in the choroidal epithelium as being due to fat or to hyalin. In our preparations

fat stains (Nile blue and scharlach R) failed to demonstrate the presence of fat, and hyaline stains (van Gieson) still showed them as clear spaces in the cytoplasm. Increased granulation of the cells has been noted, but we have not seen condensation of the granules at the base of the cells and rarefaction at the apexes, as has been described by other observers (Weed,[1] Pettit and Girard,[6] Meek,[11] etc.).

CHANGES IN THE EPENDYMA

The ependymal lining is composed of a single layer of epithelial cells which are attached to the underlying substance of the brain by a very thin basement membrane (fig. 7). The cells vary in height

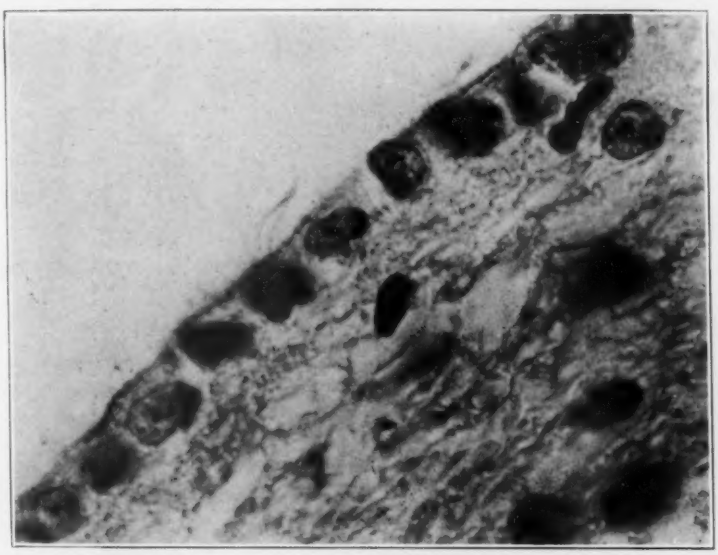

Fig. 7.—Normal ependyma. The lining membrane is uniform; in places it appears ciliated. Several small vacuoles can be seen between or below the nuclei. The basement membrane of the cells is not clearly defined. The type of cell apparently is cuboidal. In certain instances the normal ependyma may be considerably more vacuolated than is shown here. Hematoxylin and eosin stain; × 1,800.

in different parts of the ventricular system, but become more columnar as they approach the choroid plexus. Normally, the lowest type of cell measures about 5 microns, the cuboidal type from 6 to 9 microns, and the columnar type, near the pedicle of the choroid plexus, from 11 to 13 microns in height. There has been some evidence that fluid may pass normally through the ependymal lining from the brain into the ventricle or under certain conditions, such as internal hydrocephalus,

in the reverse direction. Weed,[24] in discussing the elaboration of cerebrospinal fluid, stated that "a minimal production by the ependymal cells, negligible in its significance and total amount, may occur." Wislocki and Putnam,[18] as well as Nañagas,[19] have shown that in cases of experimentally produced hydrocephalus prussian blue was precipitated in minute granules both in the cytoplasm of the ependymal cells and in the perivascular and pericellular spaces of the substance of the brain beneath. They concluded that under certain circumstances both trypan blue and prussian blue found a definite pathway of escape from the

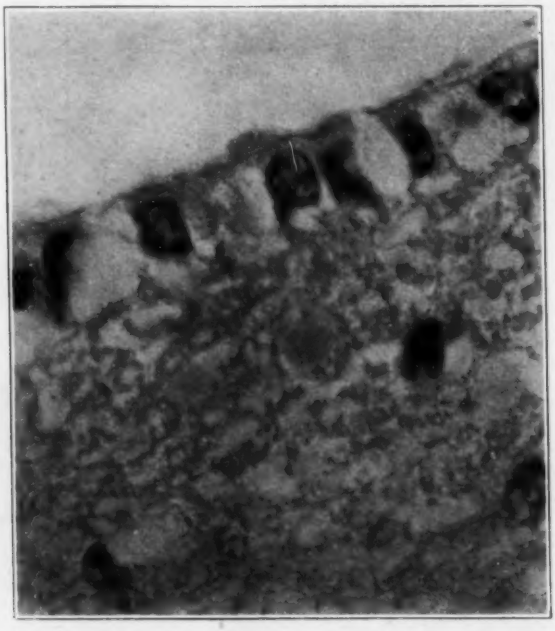

Fig. 8.—Moderate edema of the ependyma. Here moderate vacuolization of the ependymal cells is seen. The nuclei are distorted and the cells are heightened. In two places collections of fluid seem on the point of emptying into the ventricle. Considerable increase of the subependymal fluid spaces is also evident. Death occurred within thirty-six hours after injury. Hematoxylin and eosin stain; × 1,750.

ventricles, through the ependyma, into the intercellular spaces and thence into the perivascular channels.

In our series certain changes in the ependymal lining and subependymal tissue have been found (fig. 8). In the latter, varying degrees of edema occur. In certain instances the fluid spaces may be

24. Weed, L. H.: An Anatomical Consideration of the Cerebrospinal Fluid, Anat. Rec. **12**:465 (May) 1917.

moderately enlarged, in others the stroma is ballooned out to such an extent that the trabeculae or septums dividing the individual channels are broken down. The basement membrane may be ruptured by fluid pressure and under certain circumstances almost completely destroyed (fig. 9). Vacuolization of the cells is usually increased in varying degrees. The vacuoles or fluid spaces are much more numerous and larger than occur normally and may push the nuclei into eccentric positions. Not uncommonly the nuclei appear to be pushed forward toward the distal end of the cells in a palisade manner. They almost give the

Fig. 9.—Marked distortion of the edematous ependyma. Great edema of the subependymal tissue is evident. The cells are tremendously heightened and filled with fluid. The subependymal fluid spaces are dilated and wide open. The nuclei apparently were forced forward by fluid. The lining membrane is irregular and in places is broken. This represents the maximum change found in the ependyma and the subependymal tissue in this series. Death occurred forty-eight hours after injury. Hematoxylin and eosin stain; × 1,750.

appearance of having been floated up from their normal position. The height of the ependymal cells is also increased, depending largely on the amount of edema or vacuolization present. In cases of so-called "full-blown" edema of the ependymal lining, cells measuring from

30.10 to 32.25 microns have been observed. In cases of more moderate edema, cells of lessened height varying from normal to the aforementioned measurements have been seen.

Naturally, under the conditions described the outlines of the cells become irregular, often assuming most bizarre shapes. This is thought to be occasioned by the varying degrees of distention and vacuolization. In certain instances the free lining of the cells is fragmented, and if blood is present in the lateral ventricles, erythrocytes in varying degrees of degeneration may be found clinging to the free ependymal lining.

CHANGES IN THE SUBSTANCE OF THE BRAIN

Based largely on the hypothesis of a direct connection of the perivascular with the perineuronal and pericellular spaces—Virchow-Robin spaces—one may attempt to explain certain histologic changes found in the substance of the brain following injuries to the head. The connection between these spaces has not yet been definitely proved. This system has been called on by some to explain the mechanism of concussion. Mott [25] (1919) hypothecated that a shock transmitted to the fluid occupying the ventricles and the subdural, perivascular and pericellular spaces would be passed directly to the neurons themselves. He explained concussion as a result of this transmitted effect on the nerve cells. Cassasa [26] (1924) explained the mechanism of concussion in much the same way. He found an overfilling of the perivascular spaces with cerebrospinal fluid. He also expressed the belief that the fine fibrils as described by Mott [27] (1910), connecting the outer surface of the blood vessels with the surrounding brain, are torn by stretching and that frequently the wall of the vessel is lacerated. He explained perivascular hemorrhages in this way. He expressed the opinion that the cerebrospinal fluid is forced down the perivascular spaces from the subarachnoid spaces in a direction opposite to its usual flow and thus explained the distention of these spaces. It will be recalled that Weed [1] stated that "under certain conditions this direction of flow may be reversed so that the cerebrospinal fluid passes from the subarachnoid spaces to the nerve cells." Cassasa [26] felt that the direct physical changes thus caused in the ganglion cells of the brain might well explain the phenomenon of concussion.

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25. Mott, F. W.: War Neuroses and Shell Shock, London, Oxford University Press, 1919, pp. 4 and 5.

26. Cassasa, C. B.: Multiple Traumatic Cerebral Hemorrhages, Proc. New York Path. Soc. **24**:101 (Jan.-May) 1924.

27. Mott, F. W.: The Pathology of the Cerebro-Spinal Fluid, Lancet **2**:1 and 79, 1910.

There is probably a close analogy between the "water brain" produced experimentally by using intravenous hypotonic injections and the "wet brain" seen following severe injuries to the head. Naturally, the changes in the latter condition, while similar, would not be as marked as those which could be produced in the laboratory. Ferraro [28] (1930) recently studied the subject in rabbits. He found changes in the choroid, ependyma and tissue of the brain proper, which are practically analogous, though much more marked, than those seen after severe injuries to the head. He described increased vacuolization of the choroid plexus, and increased subependymal edema with disruption of the epithelial lining membrane. He also described increased edema of the interstitial

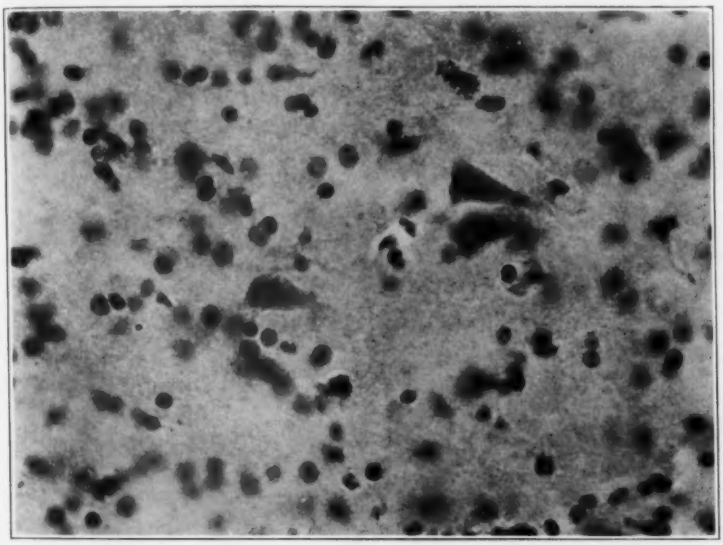

Fig. 10.—Normal substance of the brain; frozen section to eliminate artefacts. Several pyramidal cells are shown. No pericellular space is present, except as faintly indicated about one pyramidal cell at the upper right corner. At the lower right corner a vessel can be faintly seen, but the perivascular space is not evident. Hematoxylin and eosin stain; × 335.

tissue of the brain in various localities, as well as dilatation of the perivascular and pericellular spaces and even vacuolization of the nerve cells proper. In addition he has shown acute swelling of the glial elements (oligodendroglia and microglia), as well as pronounced swelling of the lining endothelium of the intima of certain small blood vessels.

Frozen sections have been employed in order to eliminate as far as possible the error that may be caused by uneven contraction of tissue

28. Ferraro, Armando: The Reaction of the Brain Tissue to Intravenous Injection of Hypotonic Solutions, J. Nerv. & Ment. Dis. **71**:129, 1930.

when paraffin or celloidin is used. This practically eliminates the production of artefacts (fig. 10). We have found an increase in the size of the perivascular and pericellular spaces in this series of fatal injuries to the head (fig. 11).

The question of how the fluid reaches these spaces appears to be the crux of the whole matter in seeking to explain edema of the brain from any cause. If a potential communication between the perivascular and the pericellular spaces exists, as Weed [1] would have one believe, it is conceivable that cerebrospinal fluid may be forced down the perivascular spaces in a reverse from the normal direction and thus overfill the pericellular spaces. This communication, however, has not yet been

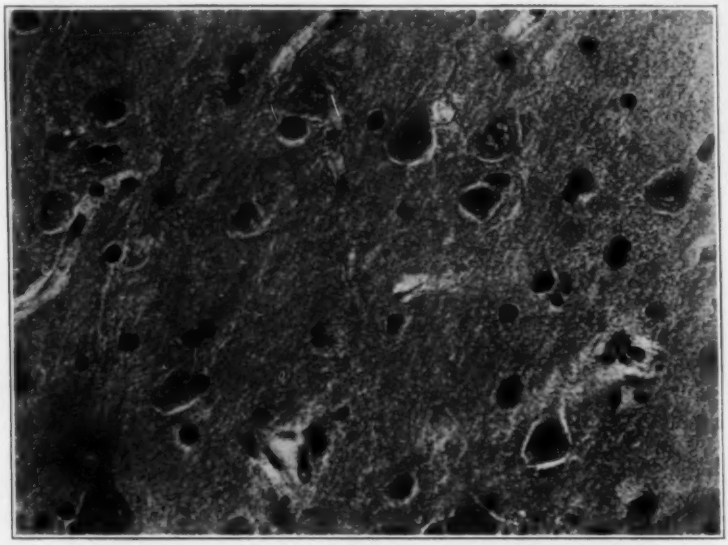

Fig. 11.—Edematous substance of the brain; frozen section to eliminate artefacts. Definite pericellular spaces are present about many cells. These spaces are enlarged and are believed to be filled with fluid following trauma. To the left and above, an enlargement of a perivascular space is clearly seen. Death occurred one hour after injury. Hematoxylin and eosin stain; × 335.

absolutely demonstrated. On the other hand, it would appear that edema of the brain may not be essentially different from edema occurring after injury in any other tissue of the body. May not fluid pass directly through the semipermeable membranes lining the smallest capillaries into these perivascular spaces, under both normal and pathologic conditions? In case of injury may not the amount of accumulating fluid be increased, thus giving rise to distention of both the perivascular and the pericellular spaces? If such a condition exists, and theoretically there is no reason why it cannot exist in the brain as in any other

tissue, no assumption of the reversal of the direction of the flow of fluid in the perivascular spaces would be necessary. One could assume that the fluid passes in increased amount directly through the semi-permeable wall of the vessel, distending the perivascular and pericellular spaces, and continues to flow back toward the subarachnoid spaces where it is absorbed in the usual channels.

In papers to follow, the changes outlined will be taken up in greater detail.

PERIOSTEUM

A LIVING BONE SUTURE *

G. W. LEADBETTER, M.D.
WASHINGTON, D. C.

Delayed union and nonunion in fractures of the long bones has for years been a fertile field for investigation and the source of much thought by surgeons specializing in conditions of the bones and joints. Many theories as to the cause of the aforementioned conditions have been advanced. Chief among them should be mentioned: (1) insufficient immobilization by improper splinting; (2) infection, either primary due to compounding of the fracture, or secondary, due to lack of aseptic technic at open reduction; (3) previous or concurrent organic disease, such as syphilis, tuberculosis, etc.; (4) general asthenia with low metabolic rate and diminution in the cellular and hemoglobin content of the blood; (5) the lowered calcium phosphorus content of the blood as determined by laboratory methods; (6) interposition of tissue, such as muscle, fascia, fat, etc.; (7) the type of suture material selected for internal fixation, such as various forms of catgut, kangaroo tendon and all metal fixative agents. After studying the numerous textbooks on fractures and dislocations, one finds that this problem of delayed union is passed over in a more or less perfunctory manner, and little attempt is made to lay emphasis on minimizing the risk of delayed union and nonunion by the selection of proper material for internal splinting and on the necessity of studying the patient as an organic whole. One should mention here the research of Petersen of Johns Hopkins, in which he studied the calcium-phosphorus content of the blood and was able to predict nonunion in those animals which showed the percentage of these chemicals below a certain level. This may explain some of these cases, but the mechanical factors of improper fixation and disturbance of circulation in the fragmented ends is another problem.

Nonunion and delayed union follow operative intervention in a far higher percentage than in the nonoperative type. For many years, without due thought and consideration, surgeons have been prone to lay the disaster at the door of the artificial suture as the inciting cause. The experimental work of Groves, published in the *British Journal of*

* Submitted for publication, June 5, 1930.

* From the Hygienic Laboratory of the United States Public Health Service, Washington, D. C.

Surgery (1913-1914), which discusses the operative intervention in fractures, leads one to the definite conclusions that:

1. Sepsis is not an infrequent result in the hands of the average surgeon.

2. Nonunion and delayed union result in about 40 or 50 per cent of all fractures so treated. This is due to the interference of the circulation in the ends of the bone fragments, affecting chiefly the meager circulation of the periosteum, and thus preventing the formation of early callus.

3. The use of absorbable sutures, absorbable pegs or absorbable bone plates frequently brings about delayed union, because these substances break, fracture or bend before sufficient callus has been thrown out to immobilize the fragments satisfactorily. Groves also stated:

> The periosteum is the product and not the mother of bone; all osteogenetic properties of the periosteum, whether in repair of fractures or in grafting, are due to the presence of the outer layer of the bone cells adherent to its deep surface. Living bone is the chief source and origin of callus which grows mainly from its outer, or periosteal surface, to a less extent from its deep or medullary surface and its cut ends.

This quotation offers the suggestion that periosteal callus is important in the early stages of bone repair.

An account of the researches of McEwen in his study of bone repair, and of Johnson in the *Journal of Bone and Joint Surgery*, July, 1927, in which both of these writers assert that the heaviest and strongest callus is thrown out by endosteal and medullary bone, gives one an excellent picture of permanent and firm union. The studies of these three men, Groves on the one side and McEwen and Johnson on the other, do not directly contradict each other, for the one is dealing with early proliferation and repair of the bone, the others with late repair and permanent union. The fixation of fragments of bone by early periosteal proliferation will aid materially in increasing circulation, and hence will act as a stimulant to the permanent and strong endosteal callus. This conclusion would seem to obtain in those cases in which large drill holes are utilized, and steel screws, kangaroo tendon or steel wire are used for fixation.

In reviewing seventy-six cases of open reduction of the long bones at the Emergency Hospital in Washington, D. C., from October, 1926, to October, 1928, one is impressed with the high percentage of nonunion and delayed union. One must remember, however, that these patients were operated on by a variety of general surgeons, and the percentage of delayed union and nonunion is probably higher than that of a well organized fracture clinic.

Only nine of these open reductions were followed by sepsis, and therefore the lack of healing of the fractures cannot be laid to improper aseptic technic. A large number of the ununited cases of fracture of both bones of the forearm is outstanding. In all of these cases, since sepsis was negligible, the delay was due either to the use of foreign suture material or to ineffectual immobilization by improper splinting. The comparison is striking, presenting 82 per cent delayed union and nonunion in the cases in which suture was employed as contrasted with 13 per cent in which it was not used. The types of suture used consisted entirely of kangaroo tendon and silver wire, no plates being used. In the analysis of this group open operation on the humerus showed no single case of delay. In fractures of the tibia, those of the lower third were conspicuous, there being 42 per cent in which suture was employed and 20 per cent in which this procedure was not used. The femur showed a delay in 25 per cent of the cases in which suture was

TABLE 1.—*Data on Seventy-Six Cases of Open Reduction of the Long Bones*

		Total	Union	Nonunion	Sepsis	Nonunion, per Cent	Total Nonunion, per Cent
Radius and ulna	Sutured	11	2	9	0	82	43
	Unsutured	15	13	2	2	13	
Tibia	Sutured	17	9	8	4	42	41
	Unsutured	5	4	1	1	20	
Humerus	Sutured	4	3	1	0	25	16
	Unsutured	2	2	0	0	0	
Femur	Sutured	12	9	3	2	25	23
	Unsutured	1	1	0	0	0	
Clavicle	Sutured	8	8	0	0	0	0
	Unsutured	0	0	0	0	0	

done, zero in those in which it was not done. Not a single case of nonunion of the clavicles was observed.

Routine roentgen studies showed no early periosteal callus and little endosteal callus at the end of several weeks. The bones were atrophied, and the fragmented ends eburnated. It is noted that the greatest percentage of nonunion occurred in bones of the forearm, although the tibia and the femur are fairly frequent offenders.

Wiring and suturing practically have been discarded because of such untoward results. The cause may partially be explained by the reasons:

1. The medullary cavities of the ulna and the radius are small.

2. The periosteum and cortex are thin.

3. The insertion of any foreign suture interferes considerably with the blood supply in the ends of the fractured fragments.

4. It would appear that good apposition of the fragments is absolutely necessary for satisfactory repair of a fracture and to minimize the chances of delayed union and of nonunion.

5. Proper fixation is one of the fundamental principles, but this is often difficult to obtain, even with immobilization of the joint above and below the break; this is especially true of the bones that are surrounded by muscles of considerable strength and length.

6. Adequate blood supply, both periosteal and medullary, should be preserved as carefully as possible. Groves, in discussing this, stated that the cortical bone adjacent to the periosteum is one of the prime factors of union, while Johnson, McEwen, Brown and Brown, and others expressed the belief that the repair is largely endosteal and medullary. In 1908, Axhausen stated that repair was both endosteal and periosteal.

7. In order to stimulate the blood supply, early mobilization of the fractured extremity is the proper procedure. This should be done as soon as is consistent with safety in maintaining the position of the fragments. It would seem, therefore, that an early callus sufficient to maintain fixation of the fragments would be ideal.

These are the cardinal principles of the treatment of fractures so that repair may take place in as short a time as possible and the dangers of nonunion may be minimized.

The necessity of internal fixation in a large number of operative cases is paramount. It would seem to follow from the foregoing facts that the sutures used heretofore, especially in the bones of the forearm and the tibia, have been unsatisfactory. Because of the importance of such a high percentage of delayed union in operative cases in which suture was used and the relative scarcity of delayed union in fractures well reduced by closed reduction, or in open reduction without suture, it would also seem that an autogenous suture of some material would be the one of election. Silver wire, catgut, kangaroo tendon, plates, bone plates, screws and bands all have a tendency to interfere with circulation, to cause absorption, to invite infection, and, in some instances, to make for insufficient immobilization. Fascia lata has been used as an autogenous suture, but it lacks the quality of stimulating early callus formation.

The qualities of the ideal bone suture should be as follows:

1. It must be strong, i. e., strong enough to maintain position of the reduced fragments in the face of the muscle pull exerted on them.

2. It should be easy to obtain with the minimum loss of function to the part from which it is excised, and should subject the patient to as small an increase in operative risk as possible.

3. It should be nonirritating in order to minimize the chances of sepsis.

4. It should be autogenous, since an autogenous tissue will not interfere with the blood supply, but rather will tend to increase it in the parts to which it is grafted.

5. It should be osteogenic by virtue of its own properties in the bone fragments in order to aid early fixation by the formation of early normal callus.

6. It should be of such a nature that it is easily inserted.

In the physiologic laboratory the tensile strength of the following sutures was taken: chromic catgut nos. 2, 3 and 4, kangaroo tendon, medium and heavy, and living periosteum. The tensile strength of silver wire, annealed iron or of twisted bronze wire was not tested,

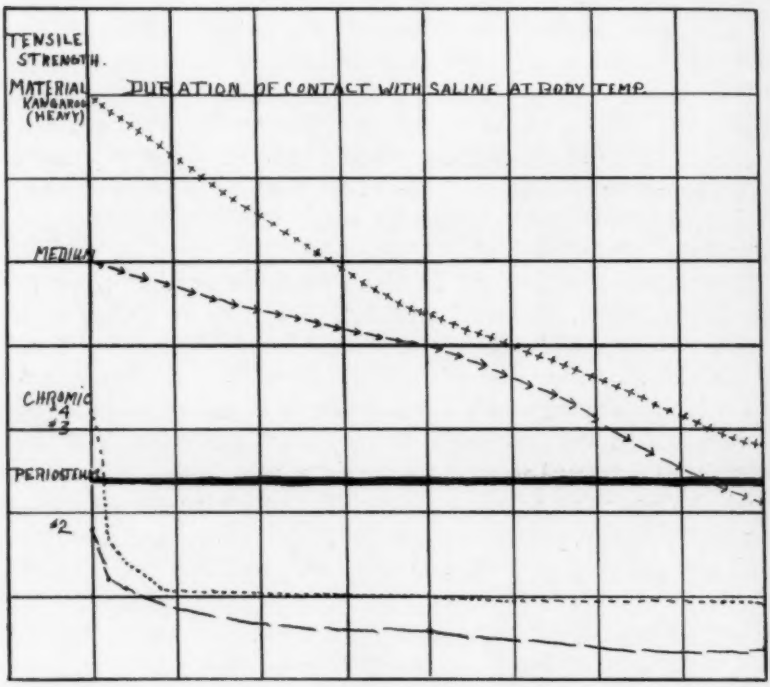

Fig. 1.—Relative tensile strength of absorbable materials placed in physiologic solution of sodium chloride at body temperature.

because their tensile strength is a definitely known quantity. It is always constant in the brand of wire used and is much greater than any of the absorbable sutures. Figure 1 shows the relative tensile strength of these absorbable materials.

The materials used were as shown. All of these substances were placed in physiologic solution of sodium chloride at body temperature and were allowed to remain there over a period of several hours, in some cases as long as forty-eight hours. The breaking strength of these substances was determined at varying intervals, the simple

dynamometer scale being used and a load of weights sufficient to rupture the sutures applied. The diameters of the various materials were obtained by a micrometer screw and a cross-section area easily determined from these figures. The tensile strength of the substances, that is, the load sufficient to rupture a cross-sectional area was computed. The results were interesting, showing that all of the absorbable sutures had a definite diminution in their tensile strength, that diminution being directly proportional to the time of contact with the physiologic solution of sodium chloride. All the catgut and kangaroo tendons were strikingly hygroscopic and increased their diameter by as much as 100 per cent in many instances. The periosteum alone survived the long period of hydration and showed no change in its tensile strength or its diameter.

Fig. 2 (rabbit 1).—A roentgenogram taken one week after fracture showing the unsplinted bone with extensive hemorrhage into the soft tissues, and no evidence of bony proliferation.

The foregoing experiment explains the conditions which are often seen following suturing of a fracture with an absorbable material. The catgut or kangaroo tendon, being hygroscopic, absorbs the tissue fluids about the site of fracture and is rapidly weakened by this physical property. Its tensile strength is much diminished, and the muscle pull is sufficient to break the fixative agent and allow a displacement of the bone fragments from forty-eight to seventy-two hours after operation. The occurrence of this phenomenon is well known to all surgeons. The periosteum when treated experimentally in this fashion shows no tendency to absorb fluids, and, since it is an autogenous tissue, should not do so in the human body; therefore its tensile strength should not be diminished in any way.

Histologically, the periosteum consists of three layers:

1. The thick fibrous coat, which contains the blood supply and lends practically all of the strength to the tissue.

2. The middle, elastic layer, containing chiefly the lymph supply. This is a thin layer and is the tissue which permits the entrance of the external blood vessels to the cortex of the bone and allows a free bathing

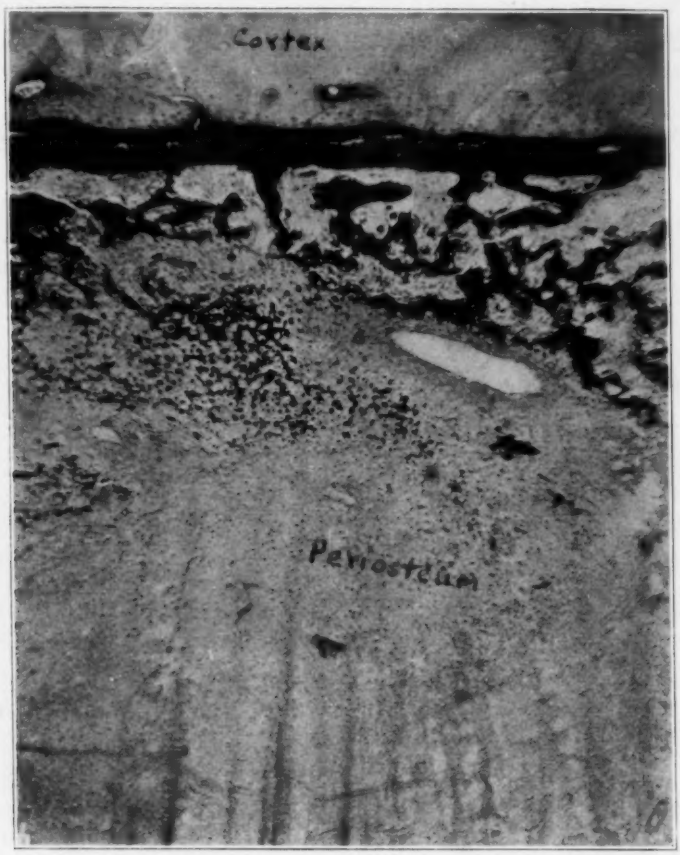

Fig. 3 (rabbit 1).—Section stained by the silver method of Lillie, seven days after operation. The black is calcium; there is early bony callus with an early calcification of the cartilage.

of the osteogenic layer in the lymph, thereby, furnishing nourishment to the osteogenic cells until they establish contact with the mother bone.

3. The inner osteogenic layer which many histologists do not feel belongs strictly to the periosteum. Whether this is true or not histologically, one can, with a little care, easily remove small scales from the

outer cortex of the bone with the fibrous periosteum. It is to these cells that we look for the osteogenic properties of this tissue.

The periosteum is an autogenous tissue and therefore nonirritating; by virtue of this same property, it is nonhygroscopic, and, as has been shown by the laboratory experiments previously mentioned, there is no tendency to diminution of the tensile strength.

The periosteum is easily obtained from the anterior surface of the tibia; here it is thicker and stronger, and hence the valuable osteoblastic cells are readily obtained. This tissue can be removed with the minimum

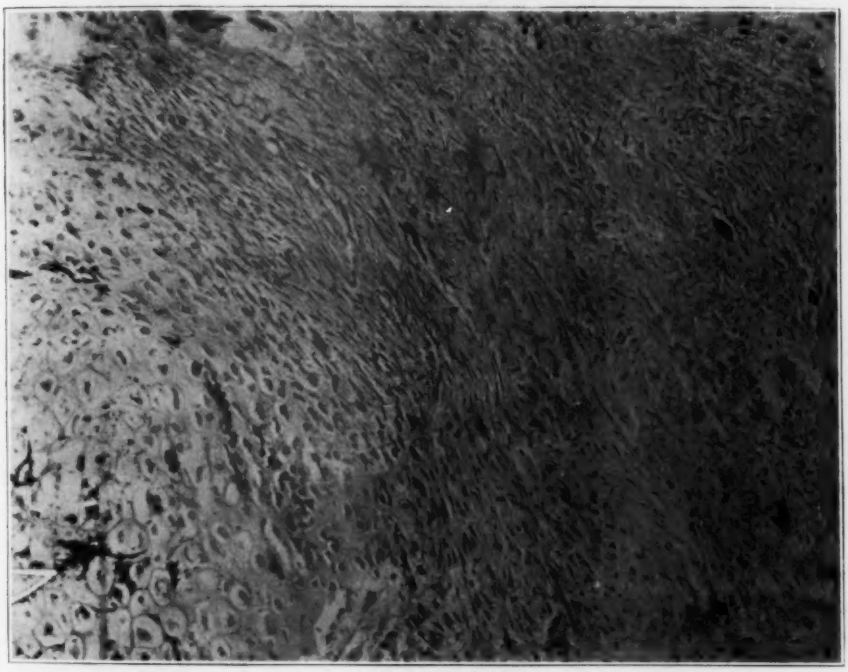

Fig. 4 (rabbit 1).—Section stained by the silver method, seven days after operation; taken at the outer portion of the callus. Some calcification is seen in the cartilage, but none in the fibrous tissue.

amount of danger to the patient, as the wounds in this region are superficial, easily dressed, and heal readily with ordinary aseptic technic. There is no more risk of an aseptic wound under these circumstances than following fascia lata excision, which is used as a living suture in a large number of plastic operations.

The periosteum is easily inserted. The technic for this type of suture is no more difficult than is the technic for any other material.

It has osteogenic properties. It is osteogenic if one is careful to remove small shavings of cortical bone with the fibrous periosteum. The

long-standing controversy as to whether periosteum is osteogenic is still apparently unsettled. Many valuable researches have been made on this subject, and many men of note have expressed diversified views. Such men as Ollier, Frankenheim, Lubenhoffer, Carrel, Axhausen, and Haas have championed the cause of periosteal proliferation in free transplant. Carrel stated that periosteum can be grown in the mediums

Fig. 5 (rabbit 1).—Section stained by the silver method, seven days after operation; higher power. The cortical bone is densely stained. Many bony lamellae are seen between which are innumerable blood spaces. The lamellae are young because their margins are irregular.

of the laboratory, and the fairly recent work of Canti, who has recorded his work by means of the cinema, leaves no doubt that the osteoblasts of the inner layer are not only monoblastic cells, but multiply rapidly in the proper surroundings. Lubenhoffer goes so far as to say that in free bone transplants the bone dies, but the periosteum lives. Haas

modified his earlier statement, and said that periosteum proliferates best when opposed to cortical bone. Those who would controvert these statements are somewhat in the minority; chief among them is Barth, who stated that all bone degenerates when freely transplanted. Brown and Brown, in a large series of experiments, arrived at the conclusion that it did not live when freely transplanted, and that it was not necessary for the life of the bone. McEwen stated that all regeneration of bone is endogenic, while Johnson is inclined to agree with the experiments of Brown and Brown that the periosteum is not essential to the life or health of bone, because the periosteal blood supply penetrates

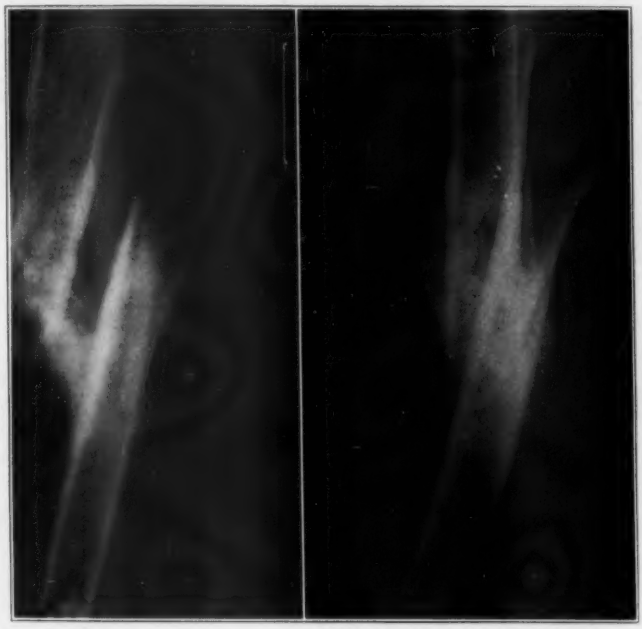

Fig. 6 (rabbit 2).—A roentgenogram taken twenty-one days after operation showing the unsplinted bone, with a bone wax medullary plug. There is marked callus, mostly periosteal.

but a small portion of the cortex. The largest blood supply comes by way of the nutrient and metaphyseal arteries.

In the present brief for the periosteal suture, it matters not whether or not periosteum regenerates when freely transplanted. One conclusion of all men who have done research on the subject of periosteum is that periosteum grows best when in contact with bone; that it regenerates early in fracture repair, thereby aiding blood supply and fixation. It is this early periosteal callus that is the conveyor of

increased blood supply to the fractured area, thus supplying increased nourishment for the formation of the strong endosteal callus which appears later. The essentials for its maximum value in its use as a suture are strength and the maintenance of strong proper fixation of the fractured bone to allow a good contact as early as possible and thus to enhance its osteogenic function in those cases in which nonunion is most probable and most common. It was from these facts and with the thought that it might be a desirable suture for certain types of fracture that the following experimental work was undertaken.

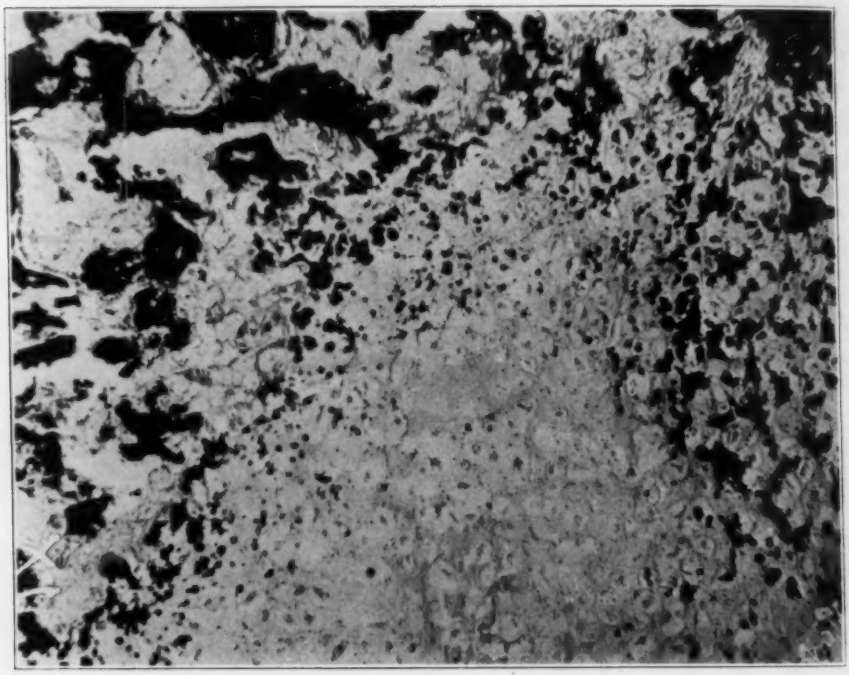

Fig. 7 (rabbit 2).—Section stained by the silver method, twenty-one days after operation; higher power magnification. There is cancellous bone, periosteal in character, and early calcification of the cartilage.

This study was made not so much to determine whether or not periosteum lived in free transplant, or whether or not it was the main factor in the healing of fractures, but rather to determine just what its reactions were under the abnormal conditions of fracture in simple cases and in those fractures in which some substance was interposed between the ends of the fragments, as well as the effect of proper and improper splinting. This study was also made to determine what occurred when a broad section of periosteum was transplanted across an area without direct bone apposition except at the ends of the graft.

MATERIAL AND METHOD OF EXPERIMENTAL WORK

In all of these experiments rabbits were used, because they were found to be less susceptible to ordinary infections due to breaks in technic, and because the period of repair of rabbit bone is short. In all cases the tibia was the bone of election. The method used was to fracture the tibia manually before exposing the bone. This allowed a sequence of events to take place such as would normally be expected following a simple fracture, namely, comminuted and other bizarre types of fracture, hemorrhage from the fragment ends and the possibility of damage and injury to the soft tissues surrounding the bone. The periosteum was utilized in different cases, as will be shown in the protocols, in order to determine just what its reaction presented. In some instances the medullary

Fig. 8 (rabbit 3).—A roentgenogram taken twenty-six days after operation showing the splinted bone; no bone wax was used. There is heavy periosteal, and some early endosteal, proliferation.

cavity was plugged with bone wax and the periosteal flap carried across the point of fracture, care always being taken to oppose the osseous surface of the periosteum at its point of contact with the cortex of the tibia. Skin closure was made in the usual way with plain 00 catgut. In some cases the leg was splinted, effectually immobilized in coaptation splints or heavy adhesive plaster casts; in others it was bandaged loosely with gauze. The animals were allowed to move about freely. In no case was there any evidence of sepsis at autopsy. These rabbits were all healthy and had not been used for any other experimental purposes. Roentgenograms were taken of all the rabbits on which autopsy was performed,

with the exception of rabbit 1, which was killed at one week and rabbit 4 which was killed at twelve days after operation; the others were allowed to live for three and four weeks. Longitudinal and transverse sections were made and stained by three methods: the silver impregnation method of Lillie, the hematoxylin and eosin stain, and the van Gieson.

RABBIT PROTOCOLS

RABBIT 1.—The tibia and fibula were fractured manually at the junction of the middle and upper third. The leg was not splinted, and the rabbit was killed at one week without operation.

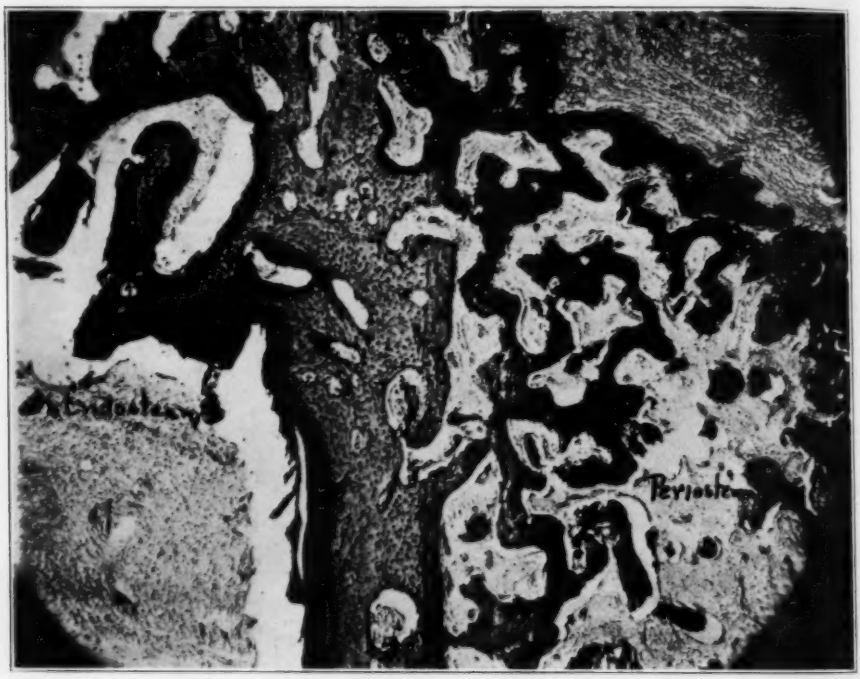

Fig. 9 (rabbit 3).—Section stained by the silver method. The cortical bone shows a very late callus, both the periosteal, the lamellae of which are densely calcified, and the endosteal, which is partly calcified. The periosteal callus is very vascular.

The roentgenogram showed an early callus formation consisting largely of hemorrhage, but with no definite bony proliferation. The fragments were in poor contact, and there was considerable angulation.

A microscopic section, stained with hematoxylin and eosin, showed a definite, early periosteal callus, with the osteoid tissue close to the bone and large masses of cartilaginous tissue which were slowly being invaded by the bone lamellae. Around the lamellae were large numbers of osteoblasts. There was no evidence whatsoever of any endosteum at this stage. The silver method of staining showed calcium salts deposited about the ends of the bones, entirely periosteal. The circulation of the proliferating periosteum was most abundant.

RABBIT 2.—The tibia and fibula were fractured at the junction of the middle and upper third. After a subperiosteal resection, which was done as completely as possible, the ends of the bone were plugged with bone wax and the usual closure made, the periosteum being allowed to fall back into as nearly a normal position as possible. The leg was not splinted in any way.

A roentgenogram taken twenty-one days after operation revealed an overriding of the fragments with no end to end contact. There was, however, a fairly considerable bony callus extending from the end of one fragment to the side of the other and also filling up the space between the dislodged fragments. It was impossible to differentiate between endosteal and periosteal callus.

Fig. 10 (rabbit 4).—A roentgenogram of the unsplinted bone taken twelve days after operation. No bone wax was used. Early periosteal, but no endosteal, callus is seen.

A microscopic section, stained by the silver impregnation method, showed a definite and thick section of osteoid tissue growing from the cortical bone. The periosteal callus under this method of staining revealed a large content of calcium salts and was extremely vascular, being filled with large blood spaces. At the outer side of this was a thick fibrous layer.

The outer coat of the periosteum in the other section taken transversely showed essentially the same picture, except that in one field it showed an early type of osteoid tissue which had not yet become calcified.

Under high power magnification, this same field in the early tissue, before calcium salts had thoroughly impregnated it, showed a definite matrix lined with calcium containing osteoblasts and all through the matrix itself were large numbers of black-stained cells.

The same sections stained by hematoxylin and eosin showed the same picture, the calcium taking the deep hematoxylin stain and being lined with a large number of osteoblasts.

In none of the sections of this rabbit was I able to pick out the formation of endosteal callus.

Rabbit 3.—This rabbit was treated in the same manner as rabbit 2 except that no bone wax was interposed. The periosteum was resected at its inferior

Fig. 11 (rabbit 4).—Section showing early periosteal callus adjacent to the cortical bone with large blood spaces. While the calcification is heavy, the lamellae are immaturely developed.

and superior attachments, the ends reversed and inserted in drill holes in either fragment. The leg was firmly splinted.

A roentgenogram, taken at autopsy twenty-six days after operation, showed the bone to have thrown out a large amount of callus. It was in good line in the lateral view, but in the anterioposterior view it had some medial angulation. There was a definite bridge of periosteal callus in both the medial and lateral sides of the tibia with a filling in of the spaces between this callus and the main cortex by firm bone.

The bones were firmly united clinically, and the rabbit was able to move about normally.

Microscopic sections stained by the hematoxylin and eosin method showed a striking proliferation of the periosteal tissue which was in all regions in close contact with cortical bone, very vascular, and at some points had begun to take on the characteristic appearance of normal cortical osseous tissue. The vascularity throughout was considerable. In this section, taken from a fractured tibia which had been completely immobilized, the bone seemed to be much more mature and there were fewer osteoblasts, the bone having more nearly reached maturity. Endosteal callus had appeared.

The section stained by the silver method showed a large amount of cancellous bone, thoroughly calcified and very vascular.

Fig. 12 (rabbit 4).—Section stained with hematoxylin and eosin twelve days after operation; × 600. The invasion of fibrous tissue and fibrocartilage by bony lamellae surrounded by osteoblasts is shown.

Rabbit 4.—This animal was treated exactly as the others, and an effort was made to force muscular tissue between the periosteum and the shaft of the bone. The leg was not splinted.

A roentgenogram taken twelve days after operation showed an early beginning callus, but no bony union. Clinically, there was no union.

Microscopic sections showed a large amount of osteoid tissue. There was good contact with the shaft of the bone itself; there was no medullary proliferation. There was some cartilaginous formation which was adjacent to the osteoid tissue. In one section there was definite osteoid tissue, a large cartilaginous mass medial to which was some fibrous tissue, a blood clot and cortical bone. The medullary cavity was free from any callus formation.

RABBIT 5.—A long incision was made over the medial portion of the tibia, extending above the knee joint. A long periosteal flap was then turned upward outside the capsule of the knee joint and fastened in a drill hole just above the medial condyle of the femur. There was no bony contact of the periosteum, except at its attached ends. The leg was thoroughly splinted after the usual closure had been made. Autopsy was done twenty-eight days after operation.

A roentgenogram taken directly after autopsy showed a definite periosteal bridge extending from the upper third of the tibia, around the capsule of the joint to the lower third of the shaft of the femur.

Transverse sections made through the condyles of the femur showed the compact bone of the condyle and the cancellous structures within, the fibrous

Fig. 13 (rabbit 5).—A roentgenogram taken twenty-eight days after operation showing the splinted bone. Periosteal proliferation is seen along the line of the graft, outside of the medial capsule of the knee joint.

tissue of the capsule interposed between this condyle and a definite periosteal graft lying medial to this region.

RABBIT 6.—The tibia was fractured after open operation, and the medulla was plugged with bone wax. The periosteum was left intact except for the long incision through which the subperiosteal resection was done. This leg was not splinted. Autopsy was done twenty-eight days after operation.

A roentgenogram showed poor position and periosteal proliferation.

Transverse sections taken through the area of fracture showed no evidence of endosteal callus, but a marked periosteal reaction, rather late because of much calcification.

RABBIT 7.—This animal was treated exactly the same as rabbit 5, except that no immobilizing splint was applied.

A roentgenogram showed no calcification in the region of the transplant.

The microscopic sections showed no evidence of any periosteal graft.

Conclusions.—1. A periosteal graft, including small fragments of cortical bone, lives and proliferates when opposed to autogenous bone in situ.

2. Periosteum is an early proliferative agent in the healing of fractures.

3. Splinting affects the formation of periosteal callus materially, since periosteum is much more dense and tends to proliferate more actively in those cases which are carefully splinted and immobilized.

4. Endosteal callus appears relatively late in the healing of fractures.

5. Endosteal proliferation advances more rapidly and forms a firmer union when fixation is strong and when stimulated by an abundant, early periosteal callus.

TABLE 2.—*Data on Calcification in Seven Rabbits*

Rabbits	Time, Days	Type of Callus
I. Not splinted	7	Early periosteal, but no endosteal callus
II. Not splinted, medullary plug	21	Early periosteal reaction, calcification of cartilage, no endosteal callus
III. Splinted, no bone wax	26	Heavy periosteal, and some early endosteal callus
IV. Not splinted	12	Very early periosteal, but no endosteal callus
V. Splinted	28	Periosteal proliferation
VI. Not splinted, medullary plug	28	Late periosteal callus, well calcified, no endosteal callus
VII. Not splinted	28	No periosteal graft

FRACTURE IN HUMAN BEINGS

I have had an opportunity to attempt the periosteal suture in several cases of fracture in human beings. Because of the experimental nature of the work, care had to be taken in the selection of cases, and an attempt was made to determine whether or not the periosteum had the properties desirable for an internal suture for fractures of certain bones. Several cases of fracture of the olecranon were selected in an effort to determine the following points: (1) whether it would hold the fragments in position, (2) whether it would proliferate as a suture and (3) whether it would aid in lessening the period of fixation normal for the healing of that particular fracture.

The periosteal suture was utilized in one case of ununited fracture of the humerus to hold the fragments in apposition after a step-cut operation was attempted. It was also used in one case of delayed union in the tibia, a broad flap of the periosteum being utilized. It has been used in one case of delayed union in fracture of the ulna. In several cases of fracture of the olecranon attempts were made to use the periosteal suture.

The operative technic is that of the insertion of any suture material. The fracture itself is first thoroughly exposed; the periosteum from the fragmented ends is carefully elevated from the shaft, and the direction in which the suture is to be applied is then decided on. Drill holes are carried through the shaft in the desired direction. A long incision is then made over the flat surface of the tibia, care being taken to incise only through the skin and subcutaneous fat. One should be extremely careful to preserve intact the outer coat of the periosteum, as it is this layer which lends its strength to the suture. With a sharp knife an incision is made through all layers of the periosteum down to and including the superficial layer of cortical bone. The strip should be from three-eighths inch to one-half inch in width, and as long as is necessary for the suturing of the bone fragments under operation. With a sharp elevator the same width as the

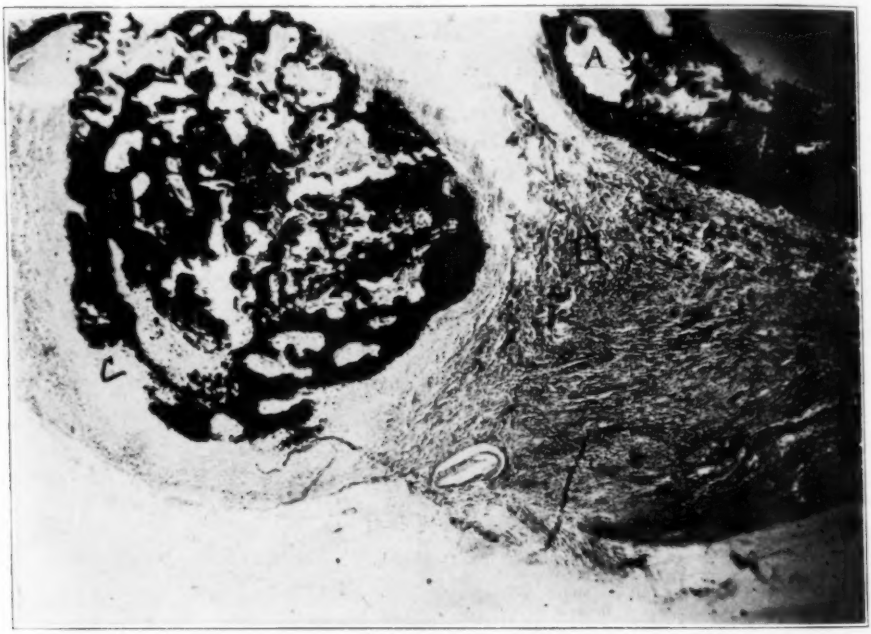

Fig. 14 (rabbit 5).—Section stained by the silver method twenty-eight days after operation. *A* shows the condyle of the femur; *B*, the capsule of the joint and *C*, the periosteal graft which has proliferated extensively.

strip to be removed, the periosteum is carefully elevated from the bone with a rotating motion of the wrist and with firm pressure to insure removal of the small fragments of the outer layer of the cortex, for it is in this tissue that the proliferative qualities exist. The osteogenic-periosteal suture is then placed in warm salt solution for preservation, and the site of the fracture prepared for its reception. Small silver probes with specially devised eyes are utilized as the carriers and the suture carefully drawn through the previously made drill holes. The method of the insertion of the suture does not matter as long as it counteracts the natural tendency for displacement of the fragments. The figure-of-eight suture is an adequate method for fixation. The suture can be readily tied if the slight amount of natural elasticity which exists in this tissue is taken up; this is

easily determined by short experience. After the suture is in place and has been tied, care should be taken to flatten out and oppose the osteogenic surface of the periosteum to the cortex of the fractured bone. If there is any doubt concerning the fixation of the knot, one suture of chromic catgut no. 2 may be passed through it and tied firmly, thereby preventing slipping. Following this, the periosteum which had previously been stripped from the bone is sutured over the transplanted graft. Closure is made in the usual accepted manner and the proper splint for the fracture under operation should be applied.

REPORT OF CASES

CASE 1.—J. G., a young colored man, had an untreated fracture of the olecranon which had occurred three months before. There was some separation

Fig. 15 (rabbit 6).—A roentgenogram of the unsplinted bone taken twenty-eight days after operation. The bone wax medullary plug was used. In the anteroposterior view there is some periosteal, but no endosteal, proliferation.

of the fragments and no bony union. He was unable fully to flex and extend the arm.

At operation the olecranon was exposed in the usual manner, and fibrous union was found to have taken place. The fibrous tissue from between the fragments was carefully removed, but no curetting of the medullary cavity was done, nor was there any resection of the eburnated ends. A periosteal graft was removed from the tibia and inserted in a side to side figure-of-eight. Union was secured in the length of time normal to a fresh fracture. Ten weeks after operation the patient had the full use of his arm with no diminution of power.

Roentgenograms taken weekly during his convalescence showed a definite and steady increase in the proliferation of the graft. No medullary callus could be made out.

CASE 2.—G., a young white woman, suffered a fracture of the olecranon in an automobile accident. There was some separation of the fragments, and operation was deemed advisable.

At operation the usual exposure was made with a periosteal suture passed through the posterior cortex of bone through the medullary canal, and tied posteriorly. Splinting consisted of fixation in a posterior metal elbow splint with the arm in about 45 degrees of flexion. Convalescence was uneventful, and at

Fig. 16 (rabbit 6).—Section stained by the silver method twenty-eight days after operation. The cortical bone is seen with an extensive, well developed periosteal callus; no endosteal callus is present.

four weeks union was complete with definite evidence of periosteal proliferation. Active physiotherapy has been started and the patient is well on the road to recovery of complete function.

CASE 3.—M. W., a young colored girl, fell off the curbing, fractured her olecranon and displaced the shaft of the ulna anteriorly.

Operation was done, and a periosteal suture inserted because of comminution of the base of the olecranon process. It was thought wise to pass the suture

from side to side through the fragments of bone. This did not afford the proper fixation for the anterior displacement of the shaft, and it would have been better in this case to have laid the suture in the figure-of-eight in order to fix both displacements.

A roentgenogram made four days after the operation showed the shaft to be displaced slightly forward. The patient was taken to the fluoroscopic room, and the shaft forced backward to its normal position.

The bone fragments were in good position with fixation fairly firm after three weeks.

CASE 4.—W. S., a colored man, fractured the olecranon and suffered slight skin abrasions in an automobile accident. Following his injury, a strepto-

Fig. 17 (rabbit 7).—A roentgenogram of the unsplinted bone twenty-eight days after operation showing no evidence of periosteal graft transplanted around the knee joint.

coccic cellulitis of the arm developed and was treated. In spite of the wide separation of the fragments, it was deemed inadvisable to operate in the face of this infection. Four weeks after the accident, when all clinical evidence of infection had subsided, open operation was attempted.

The usual method of approach was used, and a periosteal suture inserted. The olecranon was found to be rotated 90 degrees, but was easily brought into apposition and was firmly fixed with the graft. The incision over the tibia healed promptly per primum, but the incision over the elbow broke down in a few days and discharged the entire olecranon process. The infection evidently

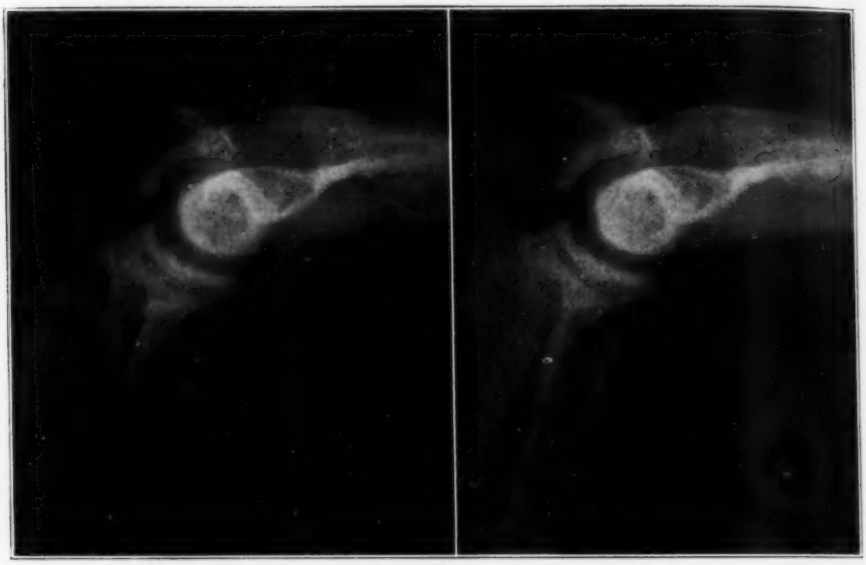

Fig. 18 (case 3).—Roentgenogram taken before operation showing separation of the fragments and comminution of the upper end of the lower fragments.

Fig. 19 (case 3).—Roentgenogram taken ten days after operation showing the suture in place, with good apposition and firm fixation.

had destroyed the graft, and the olecranon process, which was obviously necrotic bone at the time of operation, was promptly thrown off as a foreign body. After the evulsion of this fragment the wound healed, and at this date no further procedure has been instituted.

CASE 5.—A. M., a colored woman, who one year before operation fractured her tibia at the junction of the middle and upper third, had never had complete bony union, although the leg was strong enough to allow weight-bearing, but a small amount of motion could be made out at the site of the fracture. The Wassermann reaction was negative and the calcium and phosphorus in the blood showed no abnormal changes.

Fig. 20 (case 5).—Roentgenogram taken at the time of fracture one year before operation.

The site of the fracture and several inches more of the tibia was exposed. The periosteal strip from the fractured edges of the bone and a flap as broad as the anterior surface of the tibia itself were turned up over the fracture site and sutured beneath the periosteum of the upper fragment. The attachment at one end of the flap was left intact. A small slit was made in this flap, and another was brought down over the upper fragment and sutured into the periosteum of the lower. No attempt was made to invade the medullary cavity.

A roentgenogram showed some periosteal proliferation with an increase in the medullary callus after six or seven weeks.

This patient is now able to bear her weight freely without pain and without sense of instability.

CASE 6.—A. K., a white woman, one year before operation suffered a compound fracture of the humerus. A serious infection ensued which cleared up with surgical treatment, but there was the characteristic picture of nonunion with a false elbow joint.

The roentgenogram showed the characteristic eburnated bone and a striking atrophy throughout the shaft. There was no evidence of any attempt at callus formation.

The step-cut operation was used. The atrophy of the bone was so great that the drill in passing through fractured a part of the cortex, breaking the step-cut

Fig. 21 (case 5).—Roentgenogram taken before operation showing fibrous union with good general alinement.

at its base. A periosteal suture was passed through both sides of the cortex above and below the cuts. Because the elbow could not be flexed, the patient was put up in a Thomas arm splint with no traction and with the splint at 90 degrees to the body.

Proliferation of the periosteal graft in this case was striking and early. Following this, the medullary callus proceeded to form a permanent callus. Six weeks after the operation, union was complete. Since that time the function of the elbow has been materially improved by physiotherapy, and the atrophy of the cortex is much diminished.

Fig. 22 (case 5).—Roentgenogram taken seven weeks after the flap operation showing more complete union of the tibia with periosteal proliferation. The roentgenogram is dark because of efforts to show up the periosteum.

Fig. 23 (case 6).—Roentgenogram taken before operation showing nonunion and marked atrophy of the bone.

A roentgenogram showed a slight deformity of the shaft due to the fracture of the step-cut, but the periosteal callus, which made its appearance early, undoubtedly saved this patient many weeks of invalidism by its fixative properties.

CASE 7.—M., a colored man, suffered a fracture of both bones of the forearm, the lower third of the radius and the upper third of the ulna. The radius was well reduced, but the ulna had been left in poor position and had not united. Eight weeks after the original reduction, there was no bony union in the ulna, although the radius was firm.

Fig. 24 (case 6).—Roentgenograms, lateral and anteroposterior views, taken two weeks after operation showing marked periosteal deposition and a fracture of the step-cut of the lower fragment.

At operation a periosteal suture was inserted after the bony fragments had been well opposed.

A roentgenogram taken one week after operation showed the fragments to be in good position.

Comment.—From the foregoing experimental work and the clinical cases in which operation has been performed so far, it would seem that

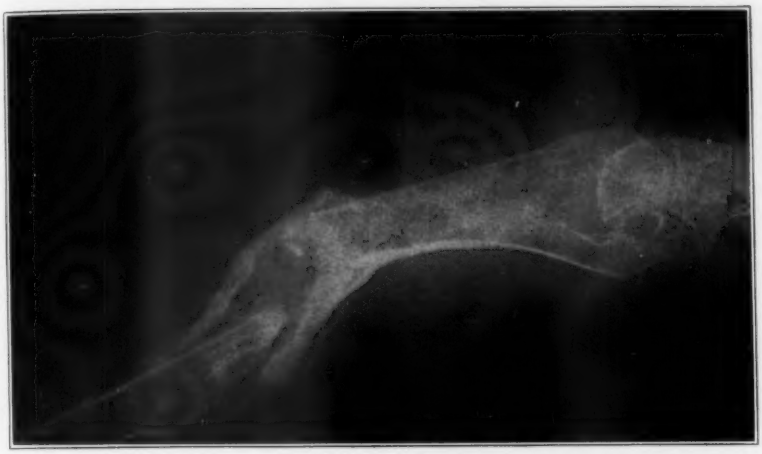

Fig. 25 (case 6).—Roentgenogram taken four weeks after operation showing heavy periosteal, with beginning endosteal, calcification.

Fig. 26 (case 6).—Roentgenogram taken five weeks after operation showing union progressing well, and good alinement of the bones.

the rôle of the periosteum as a suture offers a fertile field for investigation. All the properties of this tissue have not been fully utilized, and the various researches which have been done on bone repair have largely attempted to prove the relative value of endosteal and periosteal callus. It is not contended that the periosteum itself is the curative agent for fractures, for unquestionably the only permanent and strong repair comes through the channels of endosteal or medullary callus, but this

Fig. 27 (case 6).—Roentgenogram taken six weeks after operation showing union complete and firm by both periosteal and medullary callus. There is much less atrophy of the bone.

is relatively late in its appearance, and the necessity of a strong, non-irritating, noncirculatory disturbing suture for the purpose of producing an early fixation can readily be appreciated; even though the periosteal blood supply penetrates but a short way into the cortex. According to Johnson, this must be of material aid in early repair of fractures.

One must recognize and differentiate between early and late repair. The suture alone cannot be depended on. All the other well accepted

methods of treating open reduction should be strictly adhered to, such as proper aseptic technic, proper immobilization in splints or plaster and early physiotherapy in order to stimulate the blood supply further.

It is not argued that the use of periosteal suture should be universal and applied to fractures of all the long bones. One should select the cases with care. Periosteum is certainly not strong enough to hold firmly in fractures of such bones as the femur or the tibia in large persons, but it is most applicable to those fractures of the radius and ulna which resist one or two attempts at closed reduction and those of the humerus in which some internal fixation is necessary. In other words, the periosteal suture would seem to apply well to fractures of the long, nonweight-bearing bones. Its use seems most desirable in those cases, because fractures of the arm and of the forearm always bring to the fore the question of ultimate utility in the joints adjacent to the affected parts. Surgeons can appreciate the necessity for early mobilization of the wrist joint, the elbow joint and the shoulder joint, but frequently one is in a dilemma and fears to start motion in these joints because of the dangers of displacement. If the callus of a periosteal graft occurs as early as it appears to, one may start physical therapy at an earlier date than that ordinarily attempted in practice, for though the bones may tend to bend at the site of the injury, there is sufficient internal fixation by living osteogenic tissue to prevent a complete displacement of the fragments. Periosteal suture seems to have the further advantage that if such a displacement should occur due to an inefficient splint, one can readily reoppose the displaced fragments under the fluoroscope, still leaving the periosteal graft intact.

CONCLUSIONS

1. Autogenous periosteum has a definite tensile strength which does not vary when it is brought into contact with free body fluids.

2. It is easily obtained from the broad, anterior surface of the tibia.

3. If care is taken in the removal of the periosteum to elevate the small particles of the outer layer of the cortex, it is definitely osteogenic when placed in contact with cortical bone.

4. Periosteum proliferates best when the grafted bone is thoroughly immobilized.

5. Its proliferation in immobilized bone is rapid and early.

6. It does not interfere with the circulation in the fragmented ends, but rather increases the circulation of this region, thereby offering an aid to the formation of late callus.

7. The use of the periosteal suture allows mobilization of the fractured extremity at an early date.

The silver impregnation method, a differential stain for calcium salts, has been recently devised by Dr. Lillie of the Hygienic Laboratory, Washington, D. C. Dr. Lillie has been of invaluable assistance in studying the microscopic sections of the experimental work.

The roentgenograms and prints were all made by Mr. Robert Brown of the Emergency Hospital X-ray Department. Dr. McPeak, roentgenologist of the same institution, supplied all of the rabbits and clinical cases in which roentgenograms were made.

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A ONE-STAGE COMBINED RESECTION OF THE RECTUM *

WILLARD BARTLETT, M.D.
AND
WILLARD BARTLETT, JR., M.D.
ST. LOUIS

A good surgical operation is conceived in an understanding of the origin and method of dissemination of the disease. It is an attack that is well planned with knowledge of the anatomy involved and with the expectation of a morbidity and mortality reasonably small in relation to the relief that ensues. To the degree in which these fundamental conditions are fulfilled does the operation approach the ideal. In the light of new contributions to the knowledge of both normal and pathologic anatomy and physiology, one must at intervals revaluate one's surgical procedures. In so doing one learns why methods once thought to be theoretically sound have proved unsatisfactory in practice, and one may plan for the future on a more certain basis of fact.

The surgery of carcinoma of the rectum was for many years in the hands of two diametrically opposed groups, the Germans holding to the posterior approach and the French to the combined abdominal and perineal; the American and English tendency was rather in favor of the combined procedure. But information of outstanding practical value was reported by Miles in 1920, and by Villemin, Huard and Montagne [1] in 1925, on the lymphatic drainage of the rectum. They demonstrated that the channel of spread from the upper part of the rectum (above the last valve of Houston) is toward the abdomen, and that the channel from the lower part of the rectum is largely downward, but in part to the groin and abdomen. This work was reviewed in a masterly discussion of carcinoma of the rectum by Pfeiffer.[2] He postulated five points on which there is general agreement by the proponents of both the combined and the posterior operations:

1. In spite of the many instances of low malignancy and late metastasis observed in cancer of the rectum, permanent cures have increased in number, pari passu with wider ablation of related tissue.

2. There is no debate concerning the liability to metastatic involvement of the upward zone of spread in a certain percentage of cases.

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1. Villemin; Huard, and Montagne, quoted by Pfeiffer (footnote 2).

2. Pfeiffer, D. B.: Ann. Surg. **76**:374, 1927.

3. From the sole standpoint of cure, therefore, there is excellent reason for including this area in the bloc to be removed.

4. In most cases, complete removal of this area can be carried out only by the aid of previous intra-abdominal mobilization.

5. Those who do not practice consistent and complete removal of this zone limit their procedures for other reasons than those which have to do with permanent cure, *e. g.*, mortality, morbidity, wider applicability, less frequent necessity for abdominal anus and a feeling that their results are practically as good.

The consideration of these points has led most American surgeons of wide experience to adopt a combined operation, such as the Jones or Coffey procedure, as giving the best chance of cure. An operation the abdominal stage of which consists only of exploration and colostomy without mobilization of high lymphatic-bearing areas for subsequent removal from below cannot be considered to fulfil the requirements of the combined operation. Jones, while advocating the use of operations suitable to the strength of the individual patient, said:[3] "If we confine ourselves to an operation which can be used even on the feeble, we are not doing justice to those who can stand a more extensive operation." The newer knowledge of the lymphatics explains the observation that operations from below do not always afford sufficiently high dissection, an added indictment to the too frequently occurring terminal gangrene of the bowel, paralysis of the bladder, osteomyelitis of the sacrum and sacral hernia, chargeable to the Kraske operation and its modifications. As surgeons have familiarized themselves with the technic of the combined operation, they have tended to do it in one stage. This is desirable from the point of view of technic, since it avoids the occasional "blow-outs" occurring after the first stage. Equally important, since it applies to every patient, is the lowering of morbidity with considerable saving to the patient's purse and morale. We cannot agree with the statement that high morbidity is of no consequence in dealing with cancer. We believe that it is of considerable importance to elderly patients whose chance of living for three years has only recently risen to 50 per cent under the most favorable circumstances. The present combined operation, when done in one stage, is a long one in the best of hands, and will carry a considerable mortality in the practice of those who are called on to do it only infrequently. The chief cause of the difficulty and consequent slowness of the one-stage procedure lies in its fundamental procedure of performing the most difficult part of the abdominal stage, the deep pelvic dissection, with the rectum and anus intact. We propose to reverse the entire procedure, and by first freeing the lower segment, vastly simplify and shorten the mobilization of the structures reached through the abdomen.

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3. Jones, D. F.: Ann. Surg. **90**:675, 1929.

Before proceeding to the particulars of technic, we shall touch briefly on colostomy as a preliminary step. Reports by Rankin on large series of cases of tumors at all levels in the large intestine have shown the striking reduction in mortality and the extension of operability accomplished by colostomy and the institution of a definite regimen for the rehabilitation of certain patients. We are not committed to preliminary colostomy in all cases of cancer of the rectum and rectosigmoid. In this respect, patients are classified into three groups: At one extreme are those whose general condition is good and who do not need colostomy. Opposed to these is the group who must have colostomy because of obstruction, fixation of tumor or general depletion from pain, hemorrhage or infection. Between these extremes lies the group of patients whom one may or may not decide to explore with incidental colostomy on the suspicion of metastases to the liver or the peritoneum because of generalized tenderness or suspected free fluid. An argument in favor of preliminary colostomy in all cases is that if one performs it on a patient in whom there seems to be no necessity for it, the deferring of resection for three or four days is apt to be repaid several-fold by one's freedom to leave a clamp on the intestine much longer after resection, allowing complete primary union of the larger incision through avoidance of fecal phlegmon. We feel that attempts at extensive exploration, particularly of a site at which subsequent operation is to be performed, do not repay us in the degree to which they render more difficult the later procedure. Therefore, in the presence of infection in a rectal cancer with its well known effect on the regional lymph nodes and on the tumor itself, we look largely to the upper part of the abdomen for evidence of more than local metastasis.

When preliminary colostomy has been decided on, instead of the usual opening in the descending or sigmoid colon we make a fecal fistula in the ascending or transverse colon, since here, through the smallest opening, one can palpate the liver and detect carcinomatosis of the peritoneum and free fluid. With the colostomy placed high on the right side, the subsequent operation is performed through an abdominal wall on the pelvic colon and peritoneum undisturbed by previous manipulation and free from adhesions other than those of the disease itself. The contents of the ascending colon being largely fluid, we do not need to bring a loop of bowel outside the abdominal wall, but on these patients we perform a rapid and shockless enterostomy which differs from that employed for acute obstruction only in its location and accompanying exploration. If the diagnosis has been made previously, the colostomy is performed on the day of the patient's admission to the hospital. Its technic is as follows:

TECHNIC OF COLOSTOMY

Phenobarbital, 15 grains (0.97 Gm.), is given three hours before operation (unless the patient has acute obstruction and is vomiting). Under nitrous oxide, a vertical incision from 6 to 7 cm. long is made well within the lateral border of the right rectus. If the liver cannot be percussed below the rib margin, the upper limit of the incision should be made to within 1 cm. of the rib. The incision is carried down to the posterior sheath and the peritoneum, which are opened only enough to introduce an exploring finger. The liver may be palpated, the visceral and parietal peritoneum visualized to a limited extent by manipulation and any gush of free fluid detected. If the colon is not readily identified and brought up to the peritoneum, the incision in the posterior sheath and the peritoneum is extended to the limit of the skin incision, and the location of the colon is more readily carried out. The intestine is grasped in an Allis clamp, which is carried to the upper angle, and the peritoneum and posterior sheath are closed to within 1 cm. of the upper angle. Retraction directly upward on the Allis clamp brings the wall of the intestine into the small opening remaining in the peritoneum, to which it is fixed by four interrupted sutures of 0000 silk, such as we use for closing goiter incisions, leaving the needle on the last suture. The entire incision is then flooded with 95 per cent alcohol, and the intestine is incised just enough to admit a guttered semistiff rubber tube, 1 cm. in diameter, which is inserted to a distance of 5 or 6 cm. and transfixed with the last suture used on the intestine. The tube is cut off 2 cm. beyond the level of the skin. No sutures or dressings are used. The stitch holding the tube may be cut after three or four days or be allowed to cut through.

We have not yet had to do a secondary closure after an enterostomy performed by this technic. After a period of about ten days a Pezzar catheter is inserted into the intestine and may be worn as long as it is desired to keep the fistula open. The incision closes in rapidly, and we have had such tubes in place on three different patients at the same time, all of them keeping entirely watertight. The tube may be clamped off as desired to test the patency of the intestine below. At the present writing, one of our patients, a woman, has worn such a tube for four months, with complete comfort. The location of this incision varies somewhat with the habitus and previous intra-abdominal history of the patient. Since the transverse colon is so variable in location in the absence of intra-abdominal disease, and is usually drawn down by former appendicitis or upward by cholecystitis, judgment must be exercised as to whether one should make a high rectus incision, as here described, or a muscle-splitting incision lower down to pick up the ascending colon. The main requirement is that one reach the colon as near the liver and as far from the field of subsequent operation as possible.

The interval between colostomy and resection is regulated entirely by the patient's condition. Patients with obstructions, and depleted or bled-out patients must be fully restored. Transfusions of blood are invaluable for patients not in normal condition for any reason. Cleans-

ing of the bowel by irrigations, so far as it can ever be accomplished, takes only a few days in conjunction with a residue-free diet. We have noticed that attempts to wash the colon through a high colostomy are often unsuccessful with saline solution, owing to its absorption en route; tap water, of course, goes through readily. To the fruit juice and candy diet suggested by Rankin and Bargen, we add tea, coffee, juices of canned tomatoes and sauerkraut, fruit ices, malt tonic (containing 2 per cent alcohol) and any other alcoholic beverages, since the patients are usually elderly. Following resection, it is important that this diet be continued until the clamp has cut through.

When the patient's condition warrants, resection is carried out according to the following technic:

TECHNIC OF RESECTION

Phenobarbital (15 grains) is given three hours before operation (a smaller dose, or none at all, is used if the patient is very thin or old, or has a low blood pressure). If a fecal fistula is present, it is packed and covered. The patient is placed in a "broken-V" face position on the table, both the head and the feet being low. He is draped and prepared for the perineal stage; after all preparation is complete, the upper part of the draping is lifted and held away so that a spinal anesthetic may be inserted into the second or third lumbar interspace. After the injection of the anesthetic, the spinal needle is left in place, its stylet inserted to prevent further flow of spinal fluid, and a small soap dish or wire cage fastened over it to prevent change in its position during the course of the operation. The drapings are returned to place. The rectum is packed with iodoform gauze (1) to be used as a mold or cast for identification and (2) to prevent spilling of rectal contents in case of accidental injury. The skin around the anus is cut in a circle and sutured over with a continuous stitch. The incision is continued posteriorly in the midline up to the sacrococcygeal joint, and the coccyx is removed. The steps of the typical posterior operation are then performed; the lowest portion of the sigmoid is released by opening the peritoneum. A wide, soft rubber tube, such as would be made by closing a Penrose drain at one end, is then drawn over the specimen and anchored high up with a few sutures for the sake of safety (fig. 1). This rubber-covered mass is gently pushed up into the peritoneal cavity. The entire defect thus created is loosely packed with iodoform gauze after the necessary ligations have been made, no stiches being taken anywhere, and a large dressing is applied. The drapings are removed, the stylet is withdrawn from the spinal needle, and the patient is told to cough to ascertain whether the needle is still within the dura. A second dose of the spinal anesthetic is given, following which the needle is withdrawn. This insures one against having to use inhalation anesthesia, even though the operation takes longer than the calculated time. The patient is turned on his back and placed in the Trendelenburg position; the abdomen is opened widely from 1 to 2 cm. to the left of the midline from the pubis to the umbilicus. The tumor mass is retracted out of the abdomen and is held toward the ceiling until the conclusion of the operation (fig. 2). The customary division of the mesosigmoid is made at its attachment to the posterior wall of the pelvis and the lowest portion of the abdomen. Gross division of the mesosigmoid from the bony wall to the bowel is made at the usual point, and the upper sigmoid is drawn firmly into the upper angle of the abdominal incision.

The posterior peritoneum is completely closed, beginning with that portion first opened while the rectum was being freed from below. The abdominal wall is closed in layers without drainage; all layers are sutured as snugly as possible around the sigmoid without risking necrosis, no stitches being placed in the bowel. A rather heavy rubber-covered clamp is placed across the intestine 1 cm. from the skin, and 1 cm. beyond the clamp the sigmoid is cut through with the cautery, after the wound has been covered with petrolatum of the highest melting point, which is constantly renewed by the nurse during postoperative care. A wire cage protects the whole operative region; no dressings are used for fear of capillary

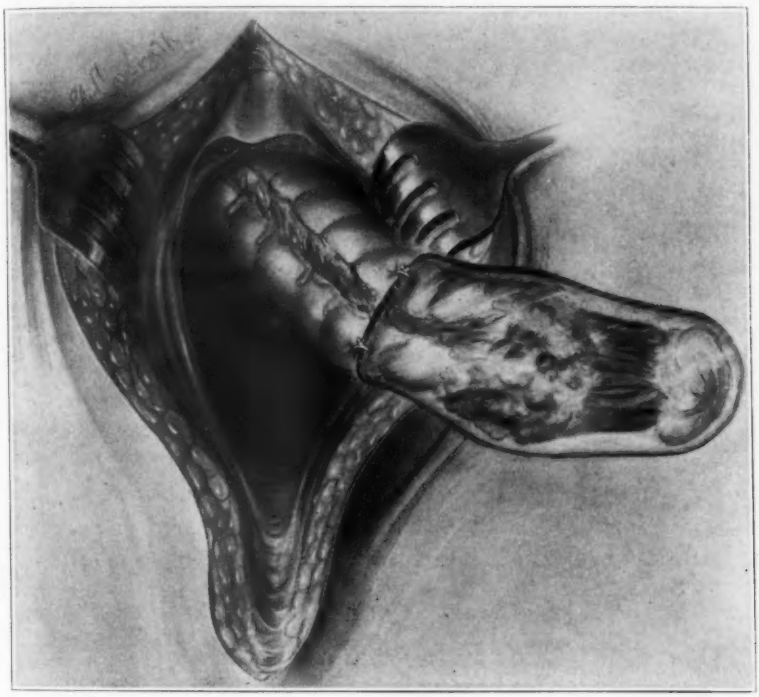

Fig. 1.—Dissection completed from below. Specimen covered with rubber.

drainage and soiling from fecal fistula, if this has been formed, or from permanent artificial anus when the clamp has cut through after several days.

This method of resection was first used, without premeditation, on a man on whom the posterior operation was being performed, as it had been decided that the cancer was too far advanced to make the combined operation worth while. His tumor was found to have canalized the rectum and to have extended so high that it could not be removed from below. The blood supply had already been sacrificed, and the best way out of the dilemma was to push the mass up into the abdomen and to

complete the operation from above. A short abstract of the history of this patient and that of a second one on whom this operation was performed are as follows:

REPORT OF CASES

CASE 1.—J. J., aged 37, a salesman, complained of the frequent passage of blood from the rectum during and between stools and occasional profuse diarrhea,

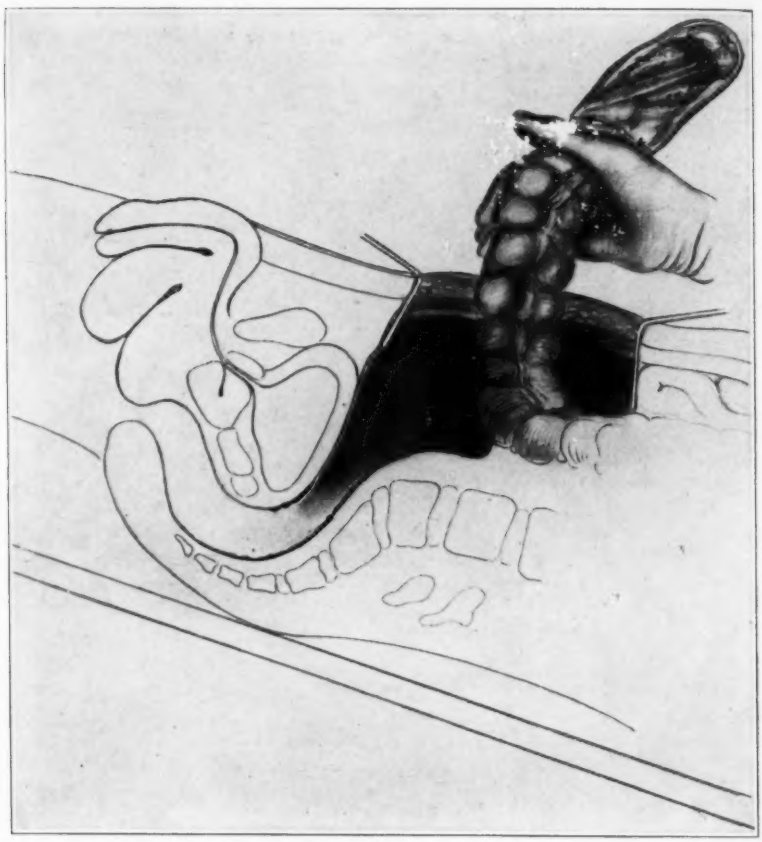

Fig. 2.—Patient in Trendelenburg position. Specimen delivered through abdominal incision and kept on traction.

the history of the condition dating from a fall. Examination showed an irregular nodular mass, ulcerated and bleeding, situated 3½ inches (8.9 cm.) above the anal orifice on the posterior rectal wall; there were tender, slightly enlarged inguinal glands. The patient entered the hospital on Nov. 9, 1924, and was operated on four days later under spinal anesthesia; the packing was removed on the second day, and patient was discharged on the sixteenth day with the abdominal incision healed but the rectal defect not yet fully granulated in. Four months later he had gained 15 pounds (6.8 Kg.) and was feeling excellent, but three months

after this he contracted influenza, during which he lost 12 pounds (5.4 Kg.); he returned for observation shortly afterward complaining of pain in the right lower quadrant and hard masses in both groins. He died a few months later.

CASE 2.—H. S., aged 41, a clerk, complained of soreness in the rectum, especially with bowel movements, slight intermittent bloody discharge and pencil stools for six weeks preceding observation. He had been treated for hemorrhoids. He had lost 8 pounds (3.6 Kg.) in two months and had had some dysuria for three weeks. Examination showed a hypertrophic, ulcerated, hard mass, 3 inches (7.6 cm.) in diameter, which bled readily, located 3 inches from the anal margin on the posterior rectal wall, largely to the left of the midline. There was considerable accompanying proctitis. An abdominal examination yielded negative results. The patient entered the hospital on Oct. 4, 1927, and was given a low residue diet and rectal irrigations. An operation was performed on October 11, and the pathologic report showed colloid carcinoma. The clamp was removed on the second postoperative day; the patient was allowed to sit up on the fourteenth day and thereafter, but his discharge from the hospital was delayed for nearly another month because of infection in the abdominal incision. His weight had returned to normal within two months after the operation, and shortly afterward he returned to work. Six months after operation he complained of pain in the buttocks and thighs, but had not lost any weight. He died of metastases a few months later.

SUMMARY

Repeated spinal anesthesia may be used in this method. By liberating the rectum and anus and bringing them, enclosed in a rubber bag, out of the abdominal wound to be used as upward traction, the most difficult part of the operation, deep pelvic dissection, is greatly simplified, since the mesosigmoid is thrown into relief and put on the stretch. It is infinitely easier to work from the depths toward oneself than in the opposite direction. Higher division of the sigmoid may be carried out, and the superior hemorrhoidal is cut at a safe point. The posterior attack is shortened, there are no drains or tubes anywhere and there is no risk of a "blow-out" below the peritoneal closure. One may perform a preliminary colostomy for exploration, for relief from obstruction, for washing out the bowel and to enable one to leave the clamp on the intestine indefinitely after resection. With the fecal fistula made in the right upper quadrant, one can perform an adequate exploration and at a subsequent operation work in an abdominal wall and pelvis undisturbed by previous recent manipulation.

Jones wrote of the abdominoperineal operation: "The third objection to the operation, the length and difficulty of it in some cases, must be admitted, and only those who are willing to accept these conditions as part of the operation should undertake it." If, as we believe, the operation here presented advances us further along any of the lines fundamental to ideal operations, it will make a sound principle available to practice in the hands of a larger number of surgeons than formerly.

SARCOMA OF THE ESOPHAGUS *

HAROLD J. DVORAK, M.D.
MINNEAPOLIS

Carcinoma of the esophagus constitutes 50 per cent of all lesions of the esophagus (Abel [1]). Sarcoma, on the other hand, is a rare condition (Ewing,[2] Kaufmann, Aschoff, Fischer [3]). Recently, there came under my observation a patient with such a lesion, and I therefore feel justified in reporting the case.

REPORT OF CASE

History.—Mrs. R. T., a white woman, aged 27, was admitted to the University Hospital on June 11, 1927, complaining of epigastric pain, diarrhea and constipation. Since March 8, 1927, she had suffered considerably with a burning epigastric pain which radiated to both sides of the thorax and up into the axillae, especially to the left. The pain had been present almost daily, and it usually lasted from one-half to six hours. She belched considerable gas and passed much flatus, but without relief. There was no qualitative or quantitative food distress. The pain often bothered her at night. She complained of being "nauseated" more or less constantly, but vomited only on three different occasions, a greenish material. She frequently missed breakfast because of the "nausea;" otherwise, she ate well. During the past three months she had lost 5 pounds (2.3 Kg.). Since the onset of her illness in March, she had also been troubled with attacks of diarrhea alternating with periods of constipation. She had eight or ten such alternate attacks. During the periods of diarrhea her bowels moved from three to four times a day. The stools were soft, but not watery. No blood or mucus was present. She also said that she became easily excited and nervous and trembled frequently; her heart would pound on such occasions.

In 1923, the patient was treated for an "ulcer of the stomach," apparently because her stools were black and tarry. At this time she did not have any epigastric symptoms. No roentgen examinations were made.

In 1924, the patient gave birth to a normal living child. There was no other pregnancy.

In 1926, she said, her stools again became black. Her physician told her that she had an ulcer of the stomach. At that time, she had vague epigastric pains and heart burn from three to four hours after meals, relieved by the taking of food. She had some nausea, but did not vomit. She was put on a diet for several weeks. There was no loss in weight, and her appetite was good. She has not noticed black stools since then.

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* From the Department of Surgery and the Cancer Institute, University of Minnesota.

1. Abel, A. Lawrence: Oesophageal Obstruction, London, Oxford University Press, 1929, p. 160.

2. Ewing, James: Neoplastic Diseases, Philadelphia, W. B. Saunders Company, 1928, pp. 277 and 907.

3. Fischer, Walther, quoted by Henke, F., and Lubarsch, O.: Handbuch der speziellen pathologischen Anatomie und Histologie, Berlin, Julius Springer, 1926, vol. 4, part 1.

During the past year she felt very weak and nervous and tired easily, until March 8, 1927, when she first noticed the symptoms already mentioned. There was no family history of malignancy and no history of venereal disease. Her dietary and hygienic habits were good.

Physical Examination.—Examination revealed a well developed and well nourished white woman, aged 27, lying quietly in bed. Her weight was 102 pounds (46.3 Kg.). The skin was warm and moist. Her eyes, ears and nose were normal. The tonsils had been removed. The thyroid was soft and moderately enlarged. There was a slight systolic bruit over it. Slight enlargement of the

Fig. 1.—Rhabdomyosarcoma of the esophagus. The tumor was soft, polypoid, yellowish white, sharply circumscribed and from 4 to 5 cm. in diameter. It sprang from the left anterolateral wall, about 5 cm. below the pharyngo-esophageal junction. It bulged into the lumen and onto the external surface of the esophagus. The latter was sutured where accidently cut.

cervical lymph nodes was present. The lungs and heart were normal. The blood pressure was 120 systolic and 78 diastolic; the pulse rate was 124. The abdomen was normal. Examination of the upper extremities on extension showed a coarse tremor of the fingers. The knee jerks were hyperactive. The basal metabolic rate was plus 25. The urine and blood were normal. Examination of the stools did not reveal blood macroscopically, microscopically or chemically. A gastric analysis gave normal results. The blood urea nitrogen and blood sugar were within normal limits. The Wassermann reaction of the blood was negative.

A diagnosis of hyperthyroidism was made. The patient was put on a compound solution of iodine, and given deep roentgen therapy to the thyroid gland.

On June 24, 1927, a roentgen diagnosis of a small prepyloric nonobstructing ulcer was made, and the patient was put on a Sippy diet. However, a roentgen examination made on July 16, 1927, failed to confirm the presence of the ulcer. Beginning on July 25, 1927, for several days she vomited her food immediately after eating. No definite cause could be found.

The patient was discharged from the University Hospital on Sept. 7, 1927. She had gained 15 pounds (6.8 Kg.), her basal metabolic rate was now minus 1, and she felt much better. She was advised to return later for further observation.

She was readmitted on Nov. 15, 1928, and said that she had felt well for some time after her discharge in September, 1927. In March, 1928, however, she had suffered a recurrence of the symptoms of a peptic ulcer. She was again put on

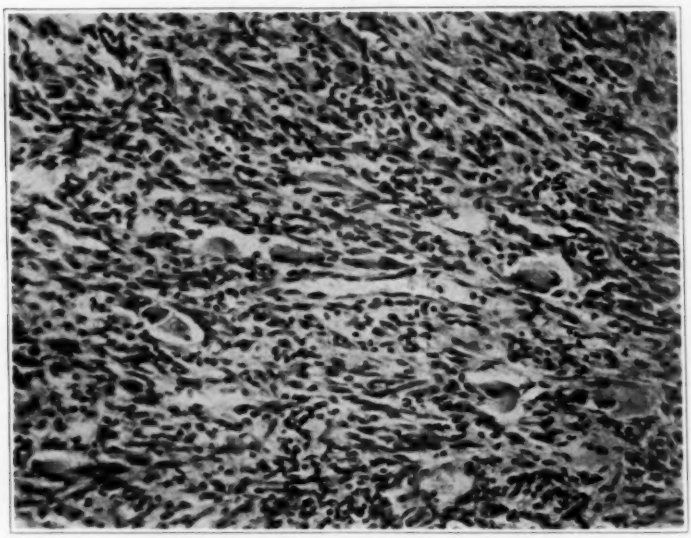

Fig. 2.—Photomicrograph of figure 1. This shows masses of spindle cells and occasional giant and muscle cells. Hematoxylin and eosin; × 90.

an ulcer diet and obtained immediate relief. However, slight pain in her stomach continued. It did not follow meals at regular intervals, but was relieved somewhat by eating and drinking. Sometimes the pain awakened her at night. Her appetite was good, and she ate all types of food. In March, 1928, she also noticed occasional gripping pains in the upper substernal region and base of her neck, and feelings of pressure in her throat, which she attributed to an ingrowing goiter. These symptoms persisted with more or less severity.

Second Examination.—This showed a well nourished young woman with negative ocular signs and moist skin. There was a coarse tremor of her fingers on extension. Other physical observations were negative. The basal metabolic rate was minus four. The blood and urine were normal. The Wassermann reaction of the blood was negative. On Nov. 26, 1928, roentgen examination of the esophagus after ingestion of a thick barium paste was negative both by fluoroscopy and on the films. It was now believed that her symptoms were not due to hyperthyroidism, although they were similar to those presented on the first

admission. She was discharged at the end of November, with a diagnosis of functional esophageal or laryngeal spasm.

On Aug. 12, 1929, she was readmitted to the hospital for the third time, and was assigned to the cancer department of Dr. A. C. Strachauer. After the patient's discharge from the hospital in November, 1928, the tight feeling in her throat, located at the level of the jugular (interclavicular) notch, grew worse. In May, 1929, she first noticed difficulty in swallowing. By July 15, 1929, she was unable to swallow anything. During the six months previous to that time she had lost 40 pounds (18.1 Kg.) in weight. Her family physician passed a stomach tube, and blood was withdrawn. The patient was admitted to the Abbott Hospital in Minneapolis, where an esophagoscope was passed by Dr. Kenneth A. Phelps. A tumor was found. Biopsy was made, and the lesion was diagnosed as spindle cell sarcoma with giant cells. Gastrostomy was performed at the Abbott

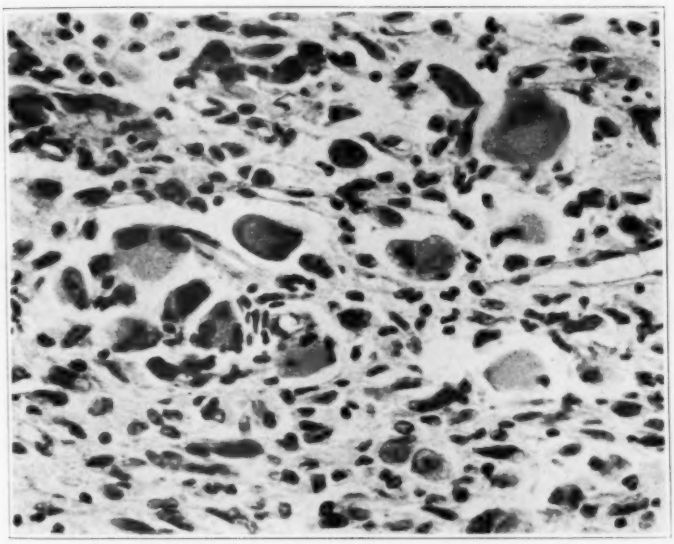

Fig. 3.—Higher power magnification of figure 2. Hematoxlin and eosin; × 250.

Hospital, and the patient was directed to the University Hospital for radiation treatment, where she now presented herself. Dr. Phelps examined the patient again on admission here, and described the lesion as follows: "There is a large necrotic tumor mass which bleeds easily and appears to spring from the left anterior esophageal wall 20 cm. from the incisor teeth, causing about 75 per cent obstruction of the lumen of the esophagus. The mass is partially covered by a white membrane."

Improvement in nutrition followed the gastrostomy, and the patient gained some relief from difficulty in swallowing. The blood showed moderate secondary anemia, with hemoglobin of 66 per cent; red blood cells, 3,500,000; white blood cells, 10,450; polymorphonuclears, 83 per cent, and lymphocytes, 17 per cent. A mass was now palpable on the left side of the neck at a level just below the larynx. Roentgenograms showed a malignant condition of the esophagus beginning at a level corresponding to about the second or third dorsal vertebra, or

about 5 cm. below the pharyngo-esophageal junction, and extending downward for about 4 cm. The malignant process displaced the esophagus to the right, suggesting pressure by an extrinsic mass.

On Aug. 22, 1929, 1,050 millicurie hours of radium were inserted into the mass by capsule through an endoscope. On September 25, a 105 per cent skin erythema dose of deep roentgen rays given in four treatments over eight days, was administered over the diseased area by Dr. Karl W. Stenstrom. Marked reaction with vomiting followed.

Her respirations became more labored, and her physical condition gradually declined. Toward the end she complained of a good deal of dyspnea. She died on November 20, probably of respiratory obstruction. It was felt that this could not be relieved because of the location of the growth. Radical extirpation of the growth was never considered, because it was believed that the lesion was extrinsic to the esophagus in origin and involved the latter only secondarily.

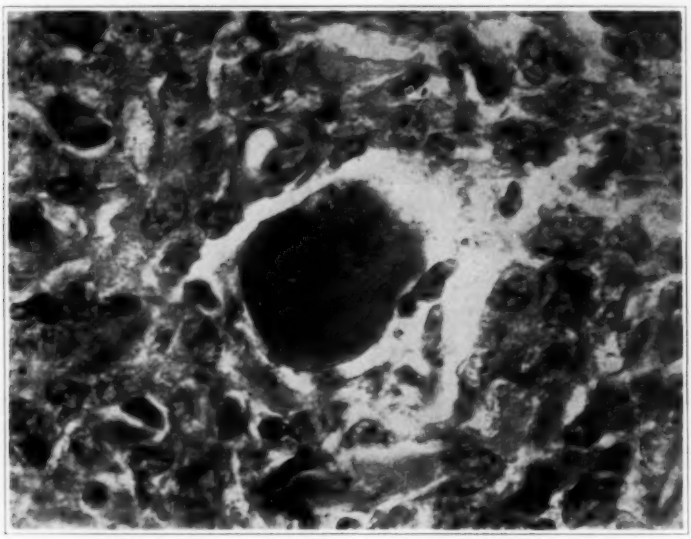

Fig. 4.—Higher power magnification of figure 3, showed a large muscle cell in the center of the field with nucleus and nucleoli. No cross-striations were demonstrated. Phosphotungstic acid stain; × 800.

Necropsy.—The postmortem examination, made by Dr. William A. O'Brien, associate professor of pathology, University of Minnesota, showed a well developed though emaciated woman. There was a gastrostomy opening present in the left upper quadrant of the abdominal wall. Five centimeters below the pharyngo-esophageal junction (lower edge of cricoid cartilage) there was a soft, yellowish-white, sharply circumscribed, polypoid tumor, from 4 to 5 cm. in diameter, springing from the left anterolateral wall of the esophagus and bulging partly into its lumen and partly from its external surface. The latter observation gave rise to the previous belief that the lesion was extrinsic, and only secondarily infiltrated the wall of the esophagus. It did not penetrate the tracheal wall, though the latter appeared slightly discolored black on its internal surface, probably from pressure. The rest of the organs were normal. There were no metastases. The para-esophageal lymph nodes were not even visibly enlarged. The lesion appeared operable.

Histologic study of the tumor under the direction of Dr. E. T. Bell, professor of pathology at the University of Minnesota, showed the constituents of the tumor to be predominantly spindle cells, some multinucleated giant cells, some round cells, fibrous connective tissue and a liberal sprinkling of muscle cells. The blood supply was moderate. The spindle cells occasionally showed mitotic figures. The muscle cells were very large, oblong or rectangular or when seen in cross-section round. The nuceli were relatively small, oval, dark staining and usually eccentrically placed. Special phosphotungstic acid stains showed a massive pink staining cytoplasm with longitudinal fibrillations. Cross-striations could not be demonstrated. This was attributed to failure of fixation of the fresh tumor tissue in the proper solution. Nevertheless, it is believed that these embryonal cells were differentiating into striated muscle of the voluntary type. The diagnosis was rhabdomyosarcoma of the esophagus.

Glinski [4] and others have shown that cross-striations in the muscle cells of these tumors are frequently difficult to demonstrate, and often cannot be found. This is especially true when the tumor process is very undifferentiated.

DISTRIBUTION AND INCIDENCE

Distribution of Sarcoma in the Digestive Tract.—Corner and Fairbank [5] studied 175 cases of sarcoma of the alimentary canal. Of this number, 14 occurred in the esophagus, 58 in the stomach, 65 in the small bowel, 20 in the cecum, 11 in the colon and 7 in the rectum.

Number of Cases in the Literature.—Chapman [6] (1877) was the first to describe esophageal sarcoma. Starck [7] (1900) collected seven cases and added two. Hacker [8] (1909) collected twenty-one cases. Hacker and Lotheissen [9] (1926) said that only thirty-eight had been described, and in some of these the origin was doubtful. Among the thirty-eight were three cases which arose mostly from the hypopharynx and only to a small extent from the esophageal entrance. Walther Fischer [3] (1926) found about fifty reported cases. Simon [10] (1928) said there were only thirty objection-free cases in the literature.

4. Glinski, L. K.: Ueber polypenförmige Mischgeschwülste des Oesophagus, Virchows Arch. f. path. Anat. **167**:383, 1902.

5. Corner, M., and Fairbank, H.: Sarcomata of the Alimentary Canal, Lancet, 1904, p. 1503.

6. Chapman, S. H.: Sarcoma of Inferior Constrictor of the Pharynx and Inlet of the Oesophagus, Am. J. M. Sc. **74**:433, 1877.

7. Starck, Hugo: Sarkome des Ösophagus, Virchows Arch. f. path. Anat. **162**:256, 1900.

8. Hacker, V.: Zur Kenntnis des Oesophagussarkoms, Mitt. a. d. Grenzgeb. d. Med. u. Chir. **19**:396, 1909.

9. Hacker, V., and Lotheissen, G.: Chirurgie der Speiseröhre, in Neue deutsche Chirurgie, Stuttgart, Ferdinand Enke, 1926, vol. 34, p. 368.

10. Simon, Hermann: Die Sarcome, in Neue deutsche Chirurgie, Stuttgart, Ferdinand Enke, 1928, vol. 43, p. 246.

Age Incidence.—The age distribution is as follows: Hacker and Lotheissen, in their thirty-eight collected cases, found only one sarcoma, a lymphosarcoma, in a very young patient. This was in Stephan's [11] case, that of a child aged 4. All the others occurred in persons between 32 and 84 years. In ten cases no age was given. Three patients were between 30 and 40 years; eight, between 40 and 50 years; seven, between 50 and 60; ten, between 60 and 70; one, between 70 and 80, and one was 84 years old. Three hypopharyngeal cases occurred in patients aged 45, 64 and 64 years, respectively. Eighty-five per cent of all sarcomas occur in persons over 40 years of age, as is true also of carcinoma. However, sarcomas occur more frequently in the young than do carcinomas, the average age of occurrence being 55 years.

Sex Incidence.—Though the sex was not always mentioned in the Hacker and Lotheissen collected series of thirty-eight cases, yet the occurrence among women was mentioned only six times. Seventy-eight per cent of the cases were among men. This observation is similar to that in carcinoma. Most authors agree regarding the relative infrequency of the condition among women as compared with men.

LEVEL OF PREDILECTION IN ESOPHAGUS

The tumor is found most frequently in the lower portion of the thoracic part of the esophagus, but gives more signs and symptoms in the cervical part. Like carcinoma, the points of predilection are usually at the level of one of the three esophageal constrictions. In thirty cases reported in the collected series of Hacker and Lotheissen, the tumor arose only seven times in the cervical portion of the esophagus, the predilection being for the lower part of the thoracic portion, just a few centimeters above the cardia of the stomach. Only occasionally do they lie in the upper thoracic part of the esophagus, according to this author. These tumors can also arise in the upper part of the pharynx and can then grow down into the esophagus. In the same series were three cases in which the tumor arose partly from the esophagus and partly from the lower portion of the pharynx. Carcinoma, on the other hand, arises most frequently in the middle third of the esophagus and least frequently in the upper third. Sarcoma, especially if it is of the circumscribed polypoid type, usually arises from the anterior wall of the esophagus and from its submucosa (Hacker and Lotheissen,[9] Fischer,[3] von Eicken,[12] Kaufmann, Aschoff and Donath [13]).

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11. Stephan, B. H.: Zur Kasuistik der Dysphagie bei Kindern (Sarcoma Oesophagie bei einem 4 Jährigen Knaben), Jahrb. f. Kinderh. **30**:354, 1890.

12. von Eicken, Carl: Ein Sarkom der Speiseröhre, Deutsche Ztschr. f. Chir. **65**:380, 1902.

13. Donath, Kurt: Beitrag zur Kenntnis der sarkomatösen Geschwülste der Speiseröhre, Virchows Arch. f. path. Anat. **194**:446, 1908.

GROSS MORPHOLOGY AND EXTENT OF PROCESS

Simon,[10] Hacker and Lotheissen [9] and Fischer [3] classified sarcomas grossly on the following basis:

1. The more circumscribed type. These have a broad base overlaid with polyps with distinct pedicles, sometimes even 16 cm. long (Borrmann [14]). The polyps consist of nodules and excrescences springing forth into the lumen and are covered by a smooth mucosal surface. These tumors are whitish or whitish yellow, hard or soft, sometimes even gelatinous, and many times superficially ulcerated. The size varies from that of an almond to that of a hen's egg. They seldom involve much of the esophageal circumference and seldom cause stenosis.

2. The diffuse infiltrating type. These are very malignant and difficult to differentiate clinically from carcinoma. They grow fast and form superficial ulcers which may be 14 cm. long. In individual places they can be more or less polypoid or cauliflower-like.

Multiple sarcomas have been seen.

Extent of the Pathologic Process.—In Gastpar's [15] case the lesion extended from the bifurcation of the trachea to the cardia of the stomach, and was both nodular and cauliflower-like. Baur's [16] melanosarcoma started at the origin of the esophagus and extended 10 cm. downward, perforating into the trachea. Other tumors, as in my case, may be no larger than from 4 to 5 cm. in diameter.

HISTOLOGY OF ESOPHAGEAL SARCOMA

Ulcerative lesions usually contain round or polyhydral cells; the polypoid lesions, spindle cells. Stephan's [11] case in a 4 year old child was a lymphosarcoma. Secondary lymphosarcoma of the esophagus has been observed by Schlagenhaufer.[17] Kaufmann said that lymphosarcomas are very rare and melanotic sarcomas most rare. Hofmann [18] described a pigmented spindle cell sarcoma; Baur, a melanosarcoma. Bertholet [19] reported a small round cell sarcoma derived from a lymph follicle.

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14. Borrmann, R.: Zwei polypöse Oesophagus Sarkome bei einem Individuum, Verhandl. d. deutsch. path. Gesellsch. **12**:121, 1908.

15. Gastpar, A.: Ein Fall von Oesophagussarkom, Centralbl. f. allg. Path. u. path. Anat. **11**:81, 1900.

16. Bauer, E. H.: Ein Fall von primären Melanom des Oesphagus, Arb. a. d. Geb. d. path. Anat. Inst. zu Tübingen **5**:343, 1904.

17. Schlagenhaufer, Friedrich: Zwei Fälle von Lymphosarcom der bronchialen Lymphdrüsen mit secundärer Lymph Sarcomatöse des Oesophagus, Virchows Arch. f. path. Anat. **164**:147, 1901.

18. Hofmann, M.: Zur Klinik der polypösen Sarkome des Oesophagus, Beitr. z. klin. Chir. **120**:201, 1920.

19. Bertholet, E.: Du sarcoma de l'oesophage, Arch. d. méd. expér. et d'anat. path. **23**:135, 1911.

Round cell sarcoma has also been described by Rolleston,[20] Starck,[7] Wegener [21] and Huismans.[22] Starck's two cases were of the large round cell type. These were not polypoid grossly and, therefore, truly malignant. Ewing said that many round cell sarcomas are nothing less than anaplastic carcinomas. Fischer stated that round cell tumors are probably either lymphosarcomas or embryonal, that is, undifferentiated, carcinomas. The spindle cell tumors are real sarcomas.

Hacker [8] (1909) found in his collected series of twenty-one cases that more than half of the cases were of the round cell or mixed cell type, the latter of which contain round cells. These are more malignant than the relatively benign spindle forms and those containing muscle fibers. Reith [23] described two cases, predominantly of the giant cell type; von Lange,[24] a spindle and large round cell type; Hacker, primarily round and spindle cells. Mixtures of these cell forms were seen by Chapman, Gastpar, Shaw [25] and Targett.[26] Howard [27] and Eppinger [28] saw, in addition to this content, smooth muscle fibers. Rarely has genuine leiomyosarcoma as reported by Hacker and Bauer [29] been described.

Spindle cell sarcomas have been reported by James,[30] Livingood,[31] Notthaft [32] and Ogle.[33] Tumors containing partly spindle cells, either large or small and partly giant cells, were described by Borrmann,

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20. Rolleston, H. D.: Sarcoma of the Oesophagus with Secondary Growths in the Bone, Tr. Path. Soc. London **44**:65, 1893.

21. Wegener: Ueber das Sarkom des Oesophagus, Inaug. Diss., Giesen, 1904.

22. Huismans, L.: Sarcoma Oesophagi, München. med. Wchnschr. **48**:2147, 1901.

23. Reith, J. W.: Ueber Zwei Fälle von primärem Sarkom des Oesophagus, Inaug. Diss., Leipzig, 1909.

24. von Lange: Primäres Oesophagussarkom, München. med. Wchnschr. **51**:411, 1904.

25. Shaw, Lauriston: Sarcoma of the Oesophagus Perforating the Trachea, Tr. Path. Soc. London **42**:90, 1891.

26. Targett, J. H.: Sarcoma of Oesophagus, Tr. Path. Soc. London **40**:76, 1889.

27. Howard, W. T., Jr.: Primary Sarcoma of the Esophagus and Stomach, J. A. M. A. **38**:392 (Feb. 8) 1902.

28. Eppinger, quoted by Hacker (footnote 8).

29. Bauer, Ervin: Zur Kasuistik der Oesophagusmyome: Ein Beitrag zur Lehre der Myome, Virchows Arch. f. path. Anat. **34**:223, 1916.

30. James, G. B.: Sarcoma of the Oesophagus with Secondary Deposit in the Tongue, Tr. Path. Soc. London **49**:91, 1898.

31. Livingood, L. E.: A Case of Sarcoma of the Esophagus, Bull. Johns Hopkins Hosp. **9**:159, 1898.

32. Notthaft, A.: Mors subitanea durch Platzen einer varicösen Oesophagusvene, München. med. Wchnschr. **42**:350, 1895.

33. Ogle, Cyril: Sarcoma of the Oesophagus, Tr. Path. Soc. London **47**:40, 1896.

Donath, von Eicken, Frangenheim,[34] Hofmann, Notthaft, Rieke[35] and Schmincke.[36]

Frattin[37] saw a lymphangio-endothelioma which constricted the entrance to the esophagus next to a bordering diverticulum. Albrecht[38] described an alveolar sarcoma. Carraro[39] saw a hemangio-endothelioma arising from the perithelium of capillaries.

Frangenheim[34] found near the cardiac end of the stomach of a woman, aged 63, a squamous carcinoma producing stenosis; above this, however, was a polypoid polymorphocellular sarcoma. The two tumors did not approach one another, being distinctly separated.

Herxheimer[40] saw in an old man a carcinoma the stroma of which simulated completely the tissue of a spindle cell sarcoma. The sarcoma had partly destroyed the carcinoma. Sokolov[41] considered this an adenosarcoma.

Pratt[42] and Lockyer[43] described a tumor which consisted partly of scirrhous carcinoma and partly of lymphosarcoma. A metastasis to the liver in this case was found to be composed purely of lymphosarcoma tissue. Socin[44] and Sommer also described carcinosarcoma of the esophagus.

The tumors in the patients of Wolfensberger[45] and Glinski[4] were considered by the authors as "rhabdomyoma" and as "mixed tumor with striated muscle," respectively. These differentiate themselves from other sarcomas in that their course is relatively benign. However, Wolfensberger's case showed a metastasis to a gland behind the cardiac end of the stomach. This was not a pure rhabdomyoma. Aschoff, also, warned that a rhabdomyoma should be treated as a sarcoma. Hacker stated that they metastasize frequently.

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34. Frangenheim, Paul: Multiple Primärtumoren, Virchows Arch. f. path. Anat. **184**:201, 1906.

35. Rieke: Ueber ein ausgedehntes medullar Sarkom des Oesophagus, Virchows Arch. f. path. Anat. **198**:526, 1909.

36. Schmincke: Diskussionsbemerkung, Verhandl. d. deutsch. path. Gesellsch. **17**:363, 1914.

37. Frattin: Due casi di tumore primitivo in diverticuli del canale digesente, Policlinico (sez. chir.), 1903, vol. 11.

38. Albrecht: Oesophagus Tumor, Wien. klin. Wchnschr. **8**:332, 1895.

39. Carraro, N.: Sopra un casa di emangioendotelioma perivascolare primitivo del'esofagus, Pathologica **50**:611, 1910.

40. Herxheimer, Gotthold: Ueber das Karzinosarkom des Oesophagus, Centralbl. f. allg. Path. u. path. Anat. **29**:1, 1918.

41. Sokolov, A.: Adenosarkom des Oesophagus, Pathologica **4**:476, 1912.

42. Pratt, quoted by Hacker and Lotheissen (footnote 9).

43. Lockyer, quoted by Hacker and Lotheissen (footnote 9).

44. Socin, Christoph: Cor.-Bl. f. schweiz. Aerzte **30**:953, 1916.

45. Wolfensberger, Rudolf: Ueber ein Rhabdomyom der Speiseröhre, Beitr. z. path. Anat. u. z. allg. Path. **15**:490, 1894.

Metastases were not demonstrable in the rhabdomyosarcoma of the esophagus reported in this paper. Histologically, the tumor in my case was identical with that in the cases of the two authors mentioned, except that myxomatous tissue was also found in the metastasis in Wolfensberger's case; also, cross-striations were demonstrated in both of the preceding cases. Wolfensberger showed drawings of the striations, but Glinski showed neither drawings nor photomicrographs of the tumor in his case. Wolfensberger interpreted the cellular elements of his tumor, other than the muscle present, as undifferentiated embryonal muscle cells, and therefore called the tumor a rhabdomyoma. Glinski preferred to interpret the same cells as types differentiating into entirely different tissue, namely, giant cells, round cells, etc., and therefore called the growth in his case mixed tumor with striated muscle. He expressed the belief that these tumors arise from undifferentiated mesenchyme displaced when the marked developmental changes occur in the ventral floor of the embryonic foregut.

Rhabdomyomas occur most frequently in the urogenital system, in the uterus, vagina, bladder, testis and, particularly, in the kidney. A favorite site for the congenital lesion is in the heart. The tumor has been reported in isolated instances in the stomach, tongue, parotid gland, breast and prostate gland and in nearly all voluntary muscles of the body (Ewing [2]). Occurrence in the esophagus is most unusual, and has been reported in the literature only twice before. This case is the third on record.

PATHOLOGIC COMPLICATIONS AND METASTASES

Polypoid spindle cell sarcomas grow slowly and destroy little tissue. There may be no secondary pathologic lesions, as in the case reported.

The infiltrating and ulcerating round cell type can quickly reach a great dimension, tend to obstruct and close the lumen, compress the trachea and lead to edema of the larynx. Destruction due to severe necrosis and gangrene is not rare, nor is bleeding or ulceration with perforation into the trachea. There may be penetration to contiguous organs, purulent pleurisy, pulmonary gangrene and eventually esophageal perforation.

Metastases are most likely to occur in the diffuse infiltrating type of round cell sarcoma. They occur early and are widely distributed to lymph nodes, inner organs and bones. They appear more quickly than in carcinoma, which, according to most authors, metastasizes late. On the other hand, metastases are predominantly lacking in the circumscribed polypoid spindle cell sarcoma. Similarly, no metastases were found in the case reported. However, the spindle cell sarcoma in Donath's [13] case did metastasize to the porta hepatis. Rhabdomyoma of

the large polypoid type, as in Wolfensberger's [45] case, may also exhibit metastases to the lymph nodes.

SYMPTOMATOLOGY AND DIAGNOSIS

Symptomatology.—The clinical symptoms closely simulate those of carcinoma. Dysphagia occurs early, and may lead to complete closure and obstruction of the esophagus. Rieke is the only author who reported that dysphagia had not occurred in his case. In Albrecht's and Carraro's cases and in Donath's second case dysphagia must be assumed to have existed, since the tumors were observed at autopsy, although nothing was reported regarding them. Sarcoma gives the appearance of slowly increasing stenosis. The sticking of food, its regurgitation and the vomiting of blood and pus are characteristic, but not constant, symptoms. Carcinoma as well as sarcoma can cause these symptoms. There is considerable pain. Its early appearance, piercing character and radiation between the shoulder blades is characteristic (Simon [10]). On the other hand, the course may be entirely symptomless, and the lesion may be discovered only incidentally post mortem. The pain occurs frequently in attacks, frequently at night, and is not related to the eating of food. Deep-seated pain may simulate the symptoms of a pulmonary affliction or even an aneurysm (Hofmann [18]). In cancer of the esophagus, actual pain is conspicuous by its absence. The sense of discomfort present is due to the slight dilatation of the esophagus from the early narrowing of its lumen, together with colicky sensations of oppression due to increased muscular contractions of the organ (Abel [1]). Thus can also be explained the symptoms of the patient in the case reported who never suffered very severe pain.

The stools may be black, due to hemorrhage, as were those of my patient. The raising of pus may simulate pulmonary abscess.

Cachexia sets in early, and earlier than in carcinoma. Von Eicken [12] attributed this to the pain, which destroys sleep at night, and which leads to loss of appetite and to an emaciation greater than that which corresponds to the stenosis. This lack of correlation between the degree of stenosis and degree of emaciation allows one to suspect sarcoma.

Diagnosis.—Sarcoma of the esophagus is clinically differentiated from carcinoma with difficulty (Simon [10]). The correct diagnosis has been made most often at necropsy (Hacker and Lotheissen [9]). Richard Cabot,[46] as a result of 3,000 postmortem examinations, arrived at the conclusion that a greater proportion of mistakes in diagnosis had been made in cases of carcinoma of the esophagus than in any other condition. This might easily include sarcoma. Proper use of a sound may elicit

46. Cabot, Richard, quoted by Abel (footnote 1).

valuable diagnostic information. Thus it can be inserted into the esophagus past a sarcoma more easily and with less injury and bleeding than past a carcinoma. This is true because of the latter's hardness and inflexibility, and because it usually involves the entire esophageal circumference, whereas sarcoma frequently involves only the anterior wall. By the resistance encountered, the level and the position of the tumor as well as the degree of stenosis may be determined. On withdrawal the sound may feel clasped more tightly at one certain point, the level of the lesion. In Gastpar's and Chapman's case no resistance was met with, in the latter because the lesion was high and partly in the pharynx.

Roentgenograms show the presence of stenosis, its level, its shape and its extent. It has been discovered that on ingestion of a contrasting material under fluoroscopy, the stream runs unimpeded down to the tumor, and here divides into two separate streams, which unite on reaching the stomach. This occurred with the slightest pathologic distortion of the esophageal wall by the tumor. Further observations must be made to determine whether such a roentgenographic observation, which is unusual for carcinoma, may be pathognomonic for sarcoma (Simon [10]).

Diagnosis can be certain only after esophagoscopy with biopsy and microscopic examination. Hacker said that his case in 1903 was the first on record in which the correct diagnosis of sarcoma of the esophagus was made during the life of the patient by biopsy section. Von Eicken saw a white necrotic membrane covering the lesion in his case. It bled easily when wiped with cotton. He thought that the condition was diphtheritic and administered antitoxin, with, of course, no result.

In making a diagnosis there must be considered, besides carcinoma, the benign tumors found on rare occasions. The following have been reported: pedicled polyps, multiple papillomas, fibromas, lipomas, myxomas, angiomas, warts and various cystic formations; also, adenomas and myomas, both of the smooth and of the striated type; also, tuberculomas and gummas.

Von Eicken [12] considered the slow growing spindle cell sarcomas operable lesions; the fast growing round cell types, inoperable; hence, the importance of exact microscopic diagnosis.

TREATMENT AND PROGNOSIS

Treatment.—The operative treatment for sarcoma in the thoracic esophagus offers little prospect of success. No successful case was found reported. Recurrence and metastases are more frequent than in carcinoma. Nevertheless, attempt at resection is justified. Such a procedure has been successful for carcinoma, as in Torek's [47] famous

47. Torek, F.: The Causes of Failure in the Operative Treatment of Carcinoma of the Oesophagus, Ann. Surg. **90**:496, 1929.

case. His patient lived thirteen years after the operation, and died of intercurrent disease. Eggers'[48] first patient with carcinoma was living at the end of one year, and his second patient was living with metastases at the end of a similar period. Lotheissen's [49] patient died from cardiac syphilis five months after surgical extirpation. The patients in Hedblom's [50] and Zaaijer's [51] successful cases lived only a few months after the operation (Torek [47]). Successful cases have also been reported by Bircher, Kümmell, Küttner, Völcker and Brun (Torek [47]). Operative cure of carcinoma of the cervical esophagus has been repeatedly accomplished (Torek). On the other hand, sarcomas located high in the esophagus have also been resected successfully. Hacker [8] was the first to do this in 1909 in a case of tumor of the anterior wall of the cervical esophagus. The microscopic nature of the tumor was later confirmed. He first did a gastrostomy, and five weeks later resected the esophagus. Six weeks later, there was recurrence of the tumor. Three months after the operation, and before the wound had completely healed, the patient died from weakness and aspiration pneumonia. Snoy[52] had a patient, aged 57, with a sarcoma involving the larynx and entrance to the esophagus. He did a tracheotomy and gastrostomy first; later he successfully performed the radical extirpation. After several months, no recurrence of the tumor followed, and only an impairment of speech and distortion of the larynx and tongue remained.

Exploratory operations in sarcomas of the esophagus have been done supposedly for other conditions. Thus one author thought his patient had a subphrenic perigastric abscess. Donath saw metastatic tumors in the abdomen, which he thought arose from the stomach.

In the literature there is a record of gastrostomy having been done three times because the patient was insufficiently nourished. Frattin's patient lived some time after such an operation; von Eicken's died soon from weakness, and Ogle's patient developed peritonitis. My patient lived four months. Von Eicken recommended gastrostomy for all patients with dysphagia. Regurgitation of injected nutrients may, however, be a serious complication.

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48. Eggers, C.: Carcinoma of the Thoracic Portion of the Oesophagus, Surg. Gynec. Obst. **50**:630, 1930.

49. Lotheissen, G.: Die Resektion der Speiseröhre, Wien. med. Wchnschr. **79**:618, 1929.

50. Hedblom, C. A.: Combined Transpleural and Transperitoneal Resection of Thoracic Esophagus, Surg. Gynec. Obst. **35**:284, 1922.

51. Zaaijer, J. H.: Erfolgreiche transpleurale Resektion eines Kardiakarzinoms, Beitr. z. klin. Chir. **83**:419, 1913.

52. Snoy: Sarkom der Pharynx-Oesophagusgrenze mit Erfolg operiert nach vorhergehender Gastrostomie, Med. Klin. **7**:58, 1911.

Perhaps more permanent cures may be effected by postoperative irradiation in sarcoma. Radium should be employed for palliation in inoperable cases to halt the destruction, probably even to make swallowing possible again and to mitigate the pain. This can be combined with the use of the galvanocautery. Spindle cell sarcomas are resistant to radium; 1,050 millicurie hours appeared insufficient in the case reported, as shown at necropsy. The dose could easily have been doubled had not perforation been feared. The effect of deep roentgen therapy on the tumor in this patient, over the previously treated thyroid area, appeared definite. Rapid proliferation was deferred, perhaps from one and a half to two years.

Prognosis.—Because of the usual extremely rapid course of the disease, the prognosis is graver than in carcinoma. Death is due to exhaustion, frequently starvation, as in the cases of Paget,[53] Chapman,[6] Targett,[26] Stephan,[11] Gastpar,[15] Glinski,[4] Wolfensberger,[45] Eppinger,[28] and Hacker's first case. It also occurs from perforation into adjacent organs, producing mediastinitis, etc. The lesion may perforate into the trachea (Shaw,[25] Wegener [21] and Baur [16]) and lead to destruction of lung tissues with abscess formation and gangrene (Rolleston,[20] Baur,[16] Livingood,[31] and Starck's [7] second case) or to intercurrent disease like pneumonia (Albrecht,[38] Rieke,[35] and Donath's [13] second case). Notthaft's [32] patient died of hemorrhage from esophageal varices caused by cirrhosis of the liver. Generalized metastases may be another cause of death. My patient died of suffocation. The duration of life is only about five or six months when dysphagia has developed.

SUMMARY AND CONCLUSIONS

Sarcoma of the esophagus is rare. Less than fifty cases have been reported in the literature; only about thirty unquestioned cases have been reported (Simon,[10] 1928). Though a disease of persons of advanced years, it occurs more frequently in the young than does carcinoma. It occurs most frequently in the lower third of the esophagus; carcinoma appears in the middle third. There are two chief types of sarcoma: the polypoid, which contains spindle cells, is relatively benign and very rarely metastasizes, and the diffuse infiltrating type, which contains round cells and early gives rise to distant metastases.

The tumor in the case herewith reported was a polypoid rhabdomyosarcoma and contained muscle cells of the striated type, spindle cells, giant cells, round cells and fibrous connective tissue. Unlike carcinoma, pain in sarcoma is often early and severe. Marked emaciation may develop long before appreciable stenosis. Dysphagia is often not the

53. Paget, Stephen: Unusual Form of Malignant Disease of the Oesophagus, Tr. Path. Soc. London **46**:46, 1895.

earliest symptom, but rather vague sensations of pressure and constriction. The condition is usually wrongly diagnosed. Most of the reported cases were correctly diagnosed only at necropsy. Diagnosis is certain only after biopsy and microscopic examination. Exact microscopic diagnosis is a valuable aid in determining operability. Sarcoma of the cervical esophagus has been resected successfully; sarcoma of the thoracic esophagus never has. The tumor in my case was refractive to 1,050 millicurie hours of radium. Deep roentgen therapy appeared to arrest the process for from one and a half to two years.

My case was unusual among the reported cases, because it was a rhabdomyosarcoma and because it occurred in the cervical region of the esophagus, in a woman and at a relatively early age. Among lesions of its type it was extraordinarily favorable to operation had it been possible to make the correct diagnosis early.

GALLBLADDER FUNCTION

I. THE CONTRACTILE FUNCTION OF THE GALLBLADDER *

I. S. RAVDIN, M.D.
AND
J. L. MORRISON, B.S.
PHILADELPHIA

Nearly a decade has passed since interest in the controversy over the emptying of the gallbladder was reawakened. During this time much has been said on both sides of the question. Any one familiar with current literature is aware that at present opinion is so divided that it seems impossible to reconcile the various views. Opinion is divided not only among clinicians, but among those who have carried out experimental work, as Levine [1] has pointed out. In fact, the major controversy at present exists in the group that has studied the mechanism of the gallbladder in the experimental laboratory.

On one side one finds Sweet,[2] Halpert,[3] Demel and Brummelkamp,[4] and Blond,[5] who are the chief advocates of the theory that the gallbladder does not empty through the cystic duct; on the other side, Elman and McMaster,[6] Whittaker,[7] Higgins and Mann,[8] Ivy and Oldberg,[9] and Boyden,[10] who believe that the gallbladder contracts to expel bile through the cystic duct.

There are also those who believe that the gallbladder is emptied through the cystic duct, but that this is accomplished by forces other than the contractile force of the musculature of the gallbladder. Winkelstein and Aschner [11] stated that respiratory movements influence emptying of the gallbladder by affecting intraperitoneal pressure.

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1. Levine, S.: Contractions of the Gallbladder as Seen in Man, Arch. Int. Med. **40**:420 (Oct.) 1927.
2. Sweet, J. E.: Internat. Clin. **34**:187, 1924; Ann. Surg. **90**:939, 1929.
3. Halpert, B.: Med. Klin. **20**:408, 1924; Am. J. Physiol. **88**:351, 1929.
4. Demel, R., and Brummelkamp, R.: Mitt. a. d. Grenzgeb. d. Med. u. Chir. **37**:515, 1924.
5. Blond, K.: Arch. f. klin. Chir. **149**:662, 1928.
6. Elman, R., and McMaster, P. D.: J. Exper. Med. **44**:151, 1926.
7. Whittaker, L. R.: Am. J. Physiol. **78**:411, 1926.
8. Higgins, G. M., and Mann, F. C.: Am. J. Physiol. **78**:339, 1926.
9. Ivy, A. C., and Oldberg, E.: Am. J. Physiol. **86**:599, 1928.
10. Boyden, E. A.: Anat. Rec. **40**:147, 1925; Surg. Gynec. Obst. **46**:30, 1928.
11. Winkelstein, A., and Aschner, P. W.: Am. J. M. Sc. **171**:104, 1926.

Graham [12] expressed the belief that the flow of bile from the liver through the common duct exerts a siphonage action on the gallbladder, while Burget [13] and Copher and Kodama [14] stated that duodenal peristalsis is the major factor which affects the flow of bile from the gallbladder.

Every one agrees on one fact, which is that, by one mechanism or another, the gallbladder is emptied of its contents, whether this is through the lymphatics, the blood vessels or the cystic duct. Workers in this laboratory had come to believe that those in favor of noncontractile function had the stronger side of the argument until about four years ago, when certain observations induced us to investigate the subject further. Data accumulated since that time have led us to believe that both processes, absorption and contraction, play a part in the emptying of the gallbladder.

MUSCULATURE

It is not to be denied that the musculature of the gallbladder is not as thick as that of the stomach, intestine or urinary bladder; but that muscle tissue is present is obvious from even cursory microscopic study of sections of the organ. The denial of sufficient muscle for function seems to be based on the fact that if nature expected bile to be forced out of the gallbladder through the cystic duct, it would have endowed this structure with a more abundant supply of muscle tissue. The answer could be easily made that if as much muscle tissue as is present is not to be used for contraction, it is a unique anatomic condition.

Muscle tissue is present; it is more abundant in some species than in others. It varies in amount; but we have not examined the gallbladder of any species which does not have some muscle tissue (fig. 1).

LYMPHATICS AND BLOOD VESSELS

Sweet,[2] Halpert,[3] and Demel and Brummelkamp [4] are exponents of the theory that the bile which enters the cystic duct leaves the gallbladder by way of the lymphatics. That absorption of certain substances—particularly water and sodium chloride, probably bile salts and perhaps cholesterol—takes place is generally believed. Whether this absorption takes place chiefly by the lymphatics or by the blood vessels is yet to be determined. That other constituents of the bile, especially pigment proteins and mucus, pass out in considerable amounts through similar pathways seems to us to be open to considerable question.

12. Graham, E.: Am. J. M. Sc. **172**:625, 1926; Surg. Gynec. Obst. **44**:153, 1927. Graham, E.; Copher, G. H., and Kodama, S.: J. Exper. Med. **44**:65, 1926.

13. Burget, G. E.: Am. J. Physiol. **74**:583, 1925.

14. Copher, G. H., and Kodama, S.: Regulations of Flow of Bile and Pancreatic Juice into Duodenum, Arch. Int. Med. **38**:647 (Nov.) 1926.

Our renewed interest in this problem arose from the fact that we have never been able to demonstrate bile pigment in the lymph from the gallbladder. Theoretically, we would expect to find it if the gallbladder bile passed in toto from the gallbladder by absorption instead of by the cystic duct.

The lymph drainage from the unobstructed gallbladder of the cat or dog did not in any instance, in many experiments, show the presence of bile pigment in amounts sufficient to demonstrate it by any method known to the physiologic chemist. It seemed possible that bile pigment

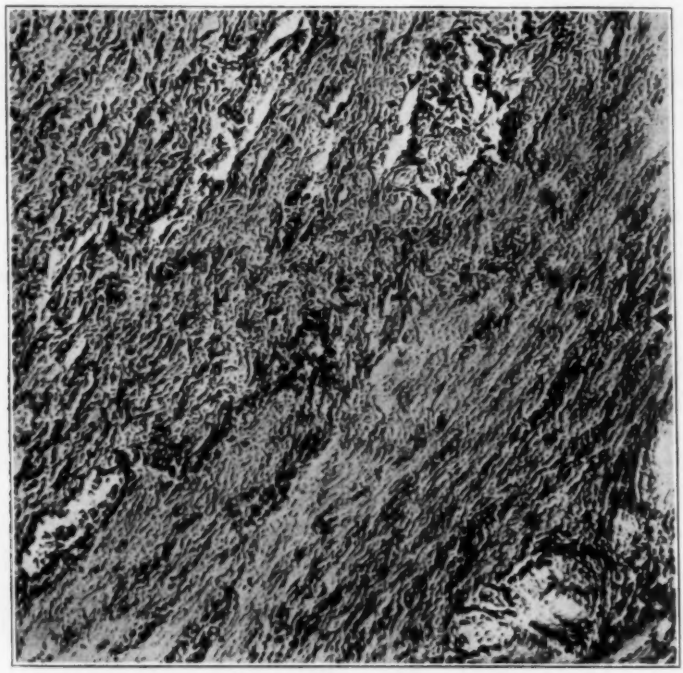

Fig. 1.—Muscularis and submucosa of the gallbladder of the dog.

might gain access to the venous return from the gallbladder, but investigations to determine this were entirely negative. We have never found enough pigment in blood taken from the cystic vein to make qualitative estimations; this is also true of the blood of the peripheral vein of the normal dog. We have introduced solutions of bilirubin into the gallbladder, with the hepatic ducts ligated, and have likewise been unable to demonstrate the disappearance of bile pigment through the lymphatics or veins. Quantitatively, we were able to recover what was introduced within experimental limits.

Dyes introduced into the gallbladder of dogs and guinea-pigs in which the common duct was intubated so as to recover any dye that escaped through the cystic duct left the gallbladder slowly through the lymph or blood vessels of the wall of the gallbladder. These dyes escaped rapidly through the cystic duct when contraction of the gallbladder was stimulated. Winkenwerder [15] has recently shown that many of the absorption studies previously done bear close scrutiny because of failure to control the experiment properly. He has, however, concluded, after a careful study, that the epithelium of the extrahepatic system, with the exception of that of the smallest bile ducts, is permeable to certain crystalloids.

We placed bile and solutions of bilirubin in an excised gallbladder, which we immersed in a Ringer-Locke solution which was kept at 38 C. We were interested in ascertaining the rapidity with which pigment would dialyze through the wall of the gallbladder. Repeated study of the Ringer-Locke solution over a three hour period failed to show that the pigment was passing through the gallbladder into the surrounding fluid.

From our studies we were led to conclude that certain constituents of bile must leave the gallbladder by channels other than those provided by the lymphatics or blood vessels, a view which has been strengthened as our work has continued.

OBSERVATIONS IN MAN

Pendergrass, Overholt and one of us (I. S. R.) were extremely fortunate last summer in observing what we believed to be rhythmic tonic contractions in a human gallbladder. The patient had previously had cholecystostomy and common duct drainage for a lesion in the head of the pancreas. During her convalescence, we introduced iodized rape seed oil into the gallbladder and observed the organ fluoroscopically. The patient was asked to stop breathing for short periods, during which we clearly saw alterations in the size and shape of the organ, which we interpreted to be the result of contraction of the gallbladder.

Pendergrass has recently obtained roentgen evidence that sodium tetraiodophenolphthalein can leave the gallbladder by way of the cystic duct. After the dye was visualized in the gallbladder and sufficient time had elapsed for its concentration in the gallbladder, as evidenced by intensification of the shadow, a meal of fat was given, and the patient was examined under the fluoroscope every few minutes. Within a short time the cystic duct was visualized, and then the common duct (figs. 2, 3 and 4). Ivy and Oldberg [9] have obtained similar roentgenograms after the injection of cholecystokinin in animals.

15. Winkenwerder, W. L.: Bull. Johns Hopkins Hosp. **46**:296, 1930.

Fig. 2.—Human gallbladder, partial concentration.

Fig. 3.—The gallbladder immediately preceding meal of fat.

It can be said that in these experiments we did not actually see the gallbladder contract. Actual observation in the intact animal is not possible, and a normal physiologic response in the anesthetized animal or human being whose abdomen is open cannot be expected. We, therefore, have studied the response of the completely isolated gallbladder to drugs, assuming that if the species that we studied responded to drugs as other smooth muscle with a similar innervation responded, we should have additional evidence that the musculature did not exist without functioning.

Fig. 4.—The gallbladder immediately after meal of fat.

THE RESPONSE OF THE ISOLATED GALLBLADDER TO DRUGS

In these studies we used the gallbladder of the dog, guinea-pig and *rhesus* monkey. The gallbladder was excised, the bile removed, and the gallbladder placed in a Ringer-Locke solution that had been well oxygenated. The temperature of the solution was maintained at 38.5 C. by a Harvey thermoregulator equipped with a telegraphic relay. The entire gallbladder was used. The fundus was attached in the lower end of the bath and the neck to a lever devised by Muschat.[16] The cystic duct was excised in all experiments.

16. Muschat, M.: J. Pharmacol. & Exper. Therap. **37**:297, 1929.

Several interesting observations were made. The contraction in response to stimulation of the guinea-pig's gallbladder was observed as long as twenty-five hours after its removal from the animal, and tonus waves for a longer time. In some instances, the gallbladder was attached so as to demonstrate circular contraction after it had been arranged for demonstration of longitudinal contractions. No difficulty was encountered in demonstrating these; two types of contractions could be obtained constantly.

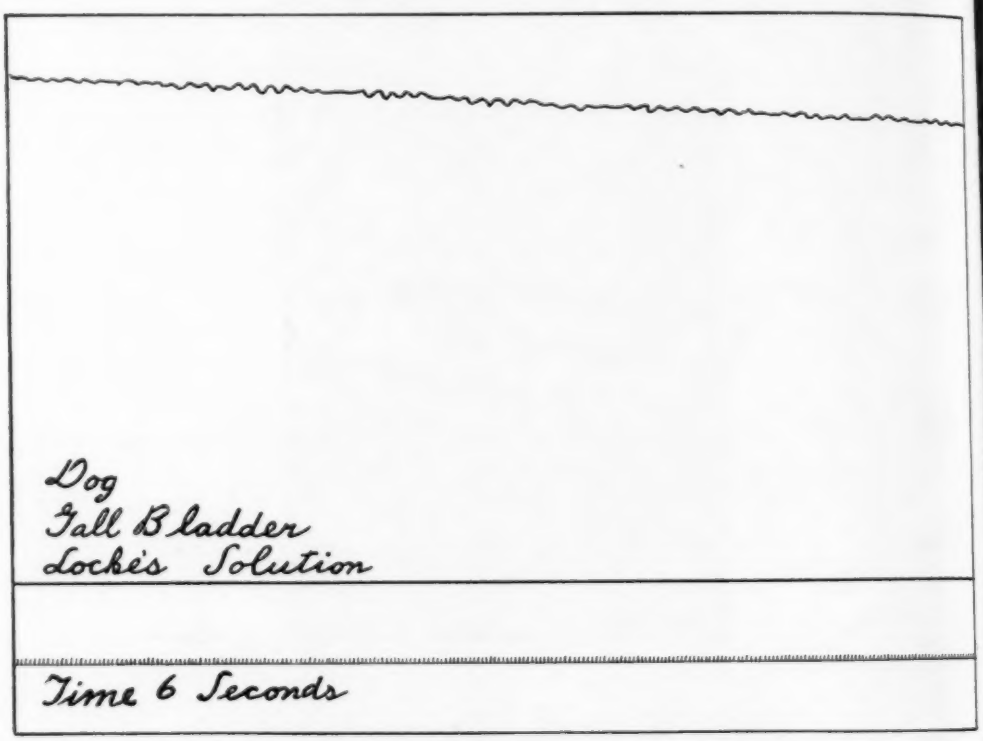

Fig. 5.—Rhythmic contractions, isolated gallbladder of the dog.

Rhythmic Contractions.—Rhythmic contractions were demonstrated in the dog, guinea-pig and *rhesus* monkey (figs. 5, 6 and 7). The rate varied somewhat, even in the same species, but usually from three to six tonus waves per minute were observed. The strength of the tonus waves varied. They were, as a rule, more forceful from fifteen to twenty minutes after immersion in the bath than they were at the beginning. The temperature of the bath affects the tonus of the gallbladder. Tonus increases up to 41 C. and then decreases. Rhythmic contractions that were not visible at 36 C. became visible between 37 and 38 C. (fig. 8).

Survival of Muscular Activity.—Tonus waves of the gallbladder of the guinea-pig were demonstrated for as long as twenty-seven hours after isolation of the gallbladder. In the dog and monkey no attempt was made to determine the total length of time over which an individual preparation would respond, but tonus waves were observed in

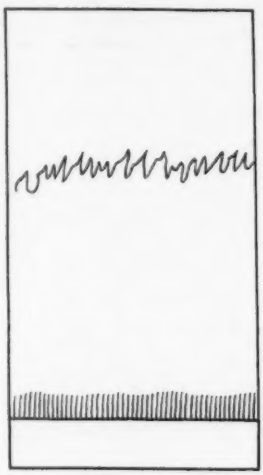

Fig. 6.—Rhythmic contractions, isolated gallbladder of the guinea-pig.

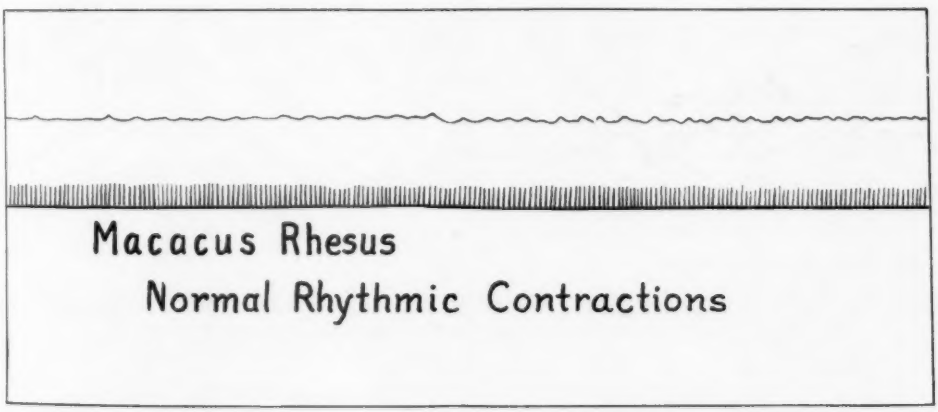

Fig. 7.—Rhythmic contractions, isolated gallbladder of the monkey.

preparations for a period of several hours. In the dog, especially, it was necessary to have from ten to fifteen minutes elapse between maximum contractions after stimulation, if similar responses were to be expected. Contractions of maximal character were obtained with the guinea-pig's gallbladder, after stimulation, twenty hours after immersion in the Ringer-Locke solution (fig. 9).

Pilocarpine.—This drug consistently caused stimulation of the isolated guinea-pig's gallbladder (figs. 10 and 11). Muscular activity following the administration of pilocarpine was paralyzed by the addi-

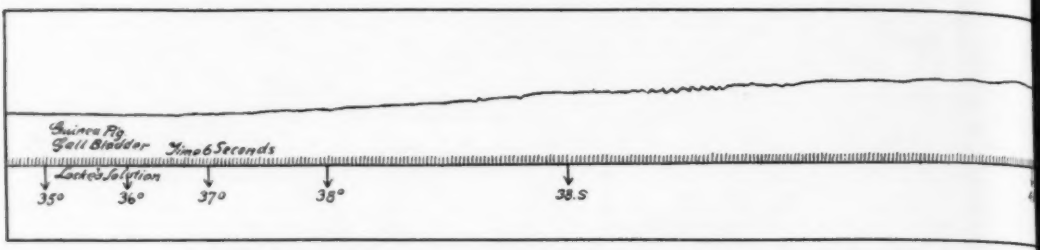

Fig. 8.—Effect of temperature on the isolated gallbladder of the guinea-pig.

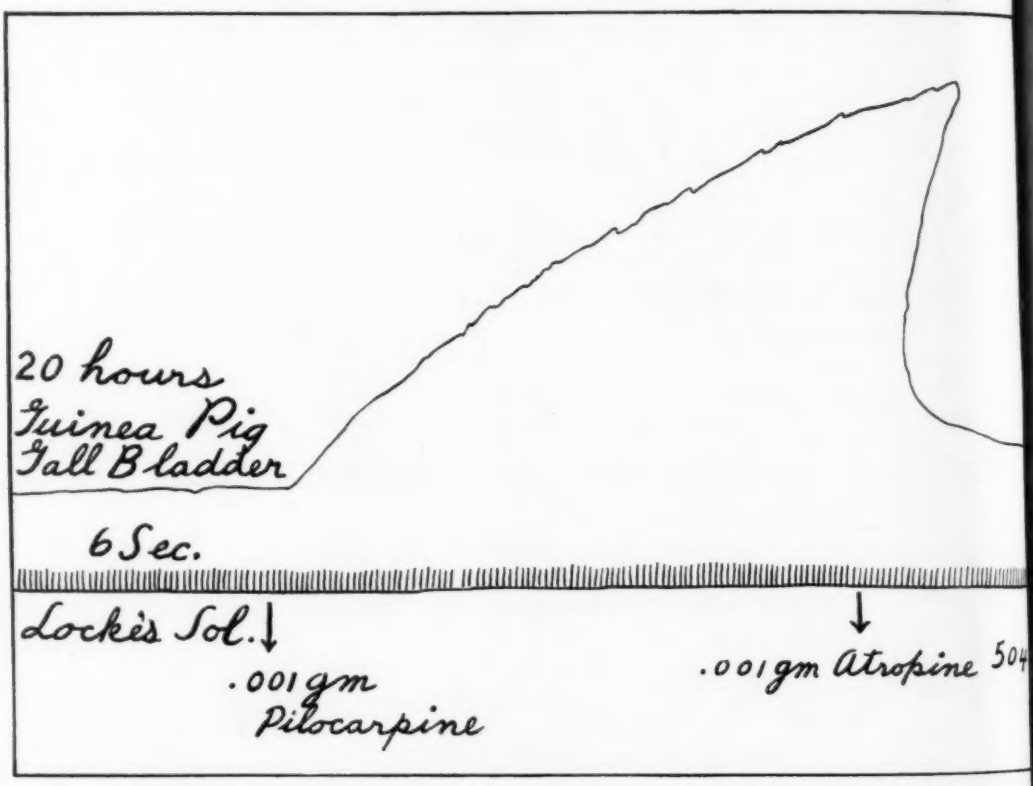

Fig. 9.—Response to pilocarpine stimulation of the guinea-pig's gallbladder twenty-four hours after isolation.

tion of atropine sulphate. The gallbladder responded actively after pilocarpine; but if it was stimulated immediately with the same drug before rhythmic contractions had returned, the contraction was of a much slower and less forceful type. Figure 12 demonstrates the

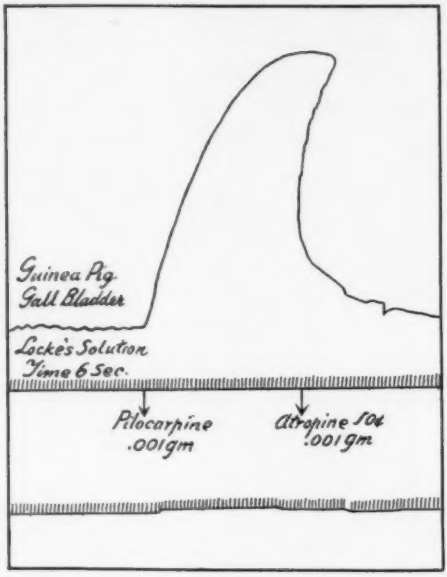

Fig. 10.—Response of the isolated gallbladder of the guinea-pig to pilocarpine.

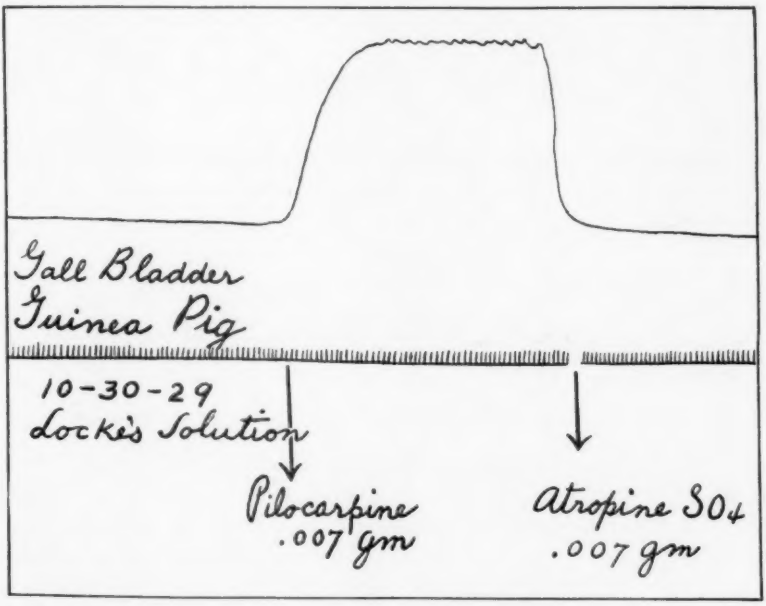

Fig. 11.—Response to pilocarpine stimulation of the isolated gallbladder of the guinea-pig.

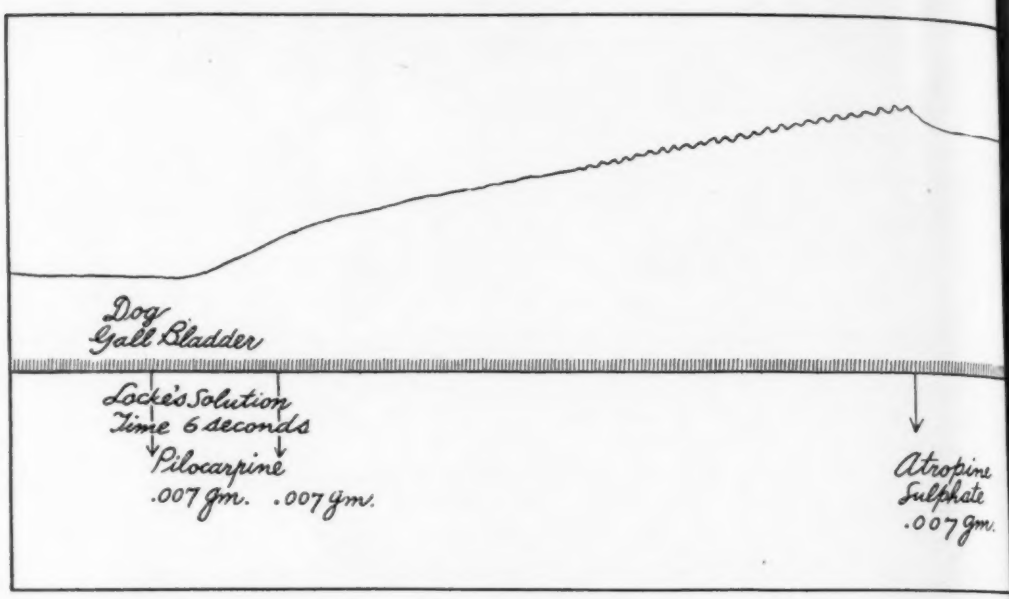

Fig. 12.—Response of the isolated gallbladder of the dog to pilocarpine stimulation.

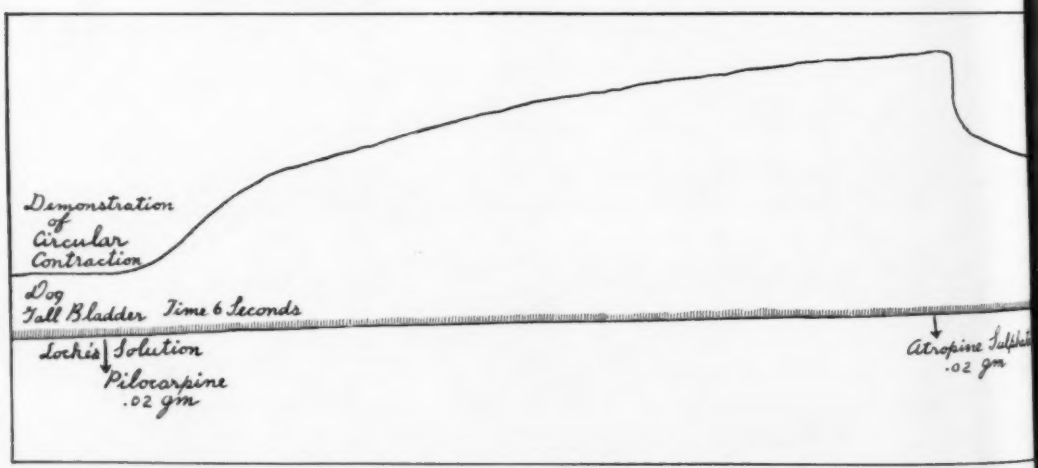

Fig. 13.—Circular contraction under pilocarpine stimulation of the isolated gall bladder of the dog.

response in the isolated gallbladder of the dog. Figure 13 illustrates the response obtained from the gallbladder when arranged to demonstrate circular contraction. Figure 14 is the tracing obtained from the gallbladder of *Macacus rhesus* after stimulation with pilocarpine.

Histamine Diphosphate.—This drug caused a response similar to that obtained with pilocarpine. It caused vigorous contraction of the isolated gallbladder with an increase in the size of the tonus waves after the solution in the bath had been changed. The response to this drug was similar to that obtained after stimulation of a smooth muscle preparation from the cornu of the virgin guinea-pig's uterus with histamine. Figure 15 is an illustration of the response of the guinea-pig's

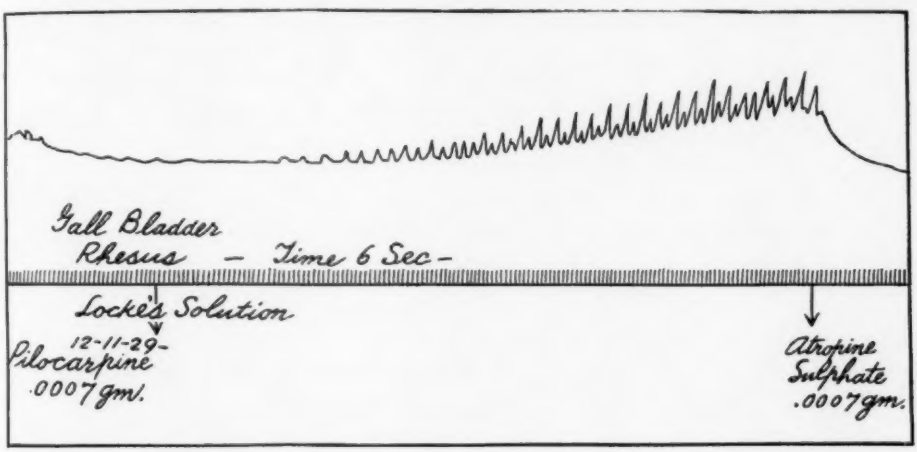

Fig. 14.—Response to pilocarpine stimulation of the isolated gallbladder of the monkey.

gallbladder to histamine twenty-four hours after isolation, while figure 16 shows the response of *Macacus rhesus* to the same drug. The dosages recorded are in terms of the salt and not in terms of histamine base.

Secretin.—Although numerous investigators have believed that the gallbladder contracts in response to a hormone, it remained for Ivy and his co-workers to bring forth strong evidence (cholecystokinin) in favor of this view. Figure 17 shows the response obtained from a guinea-pig's gallbladder with a preparation of secretin made from duodenal mucous membrane after the method of Mellanby. It shows a slow increase in tonus over a period of minutes, the time marker indicating six-second periods.

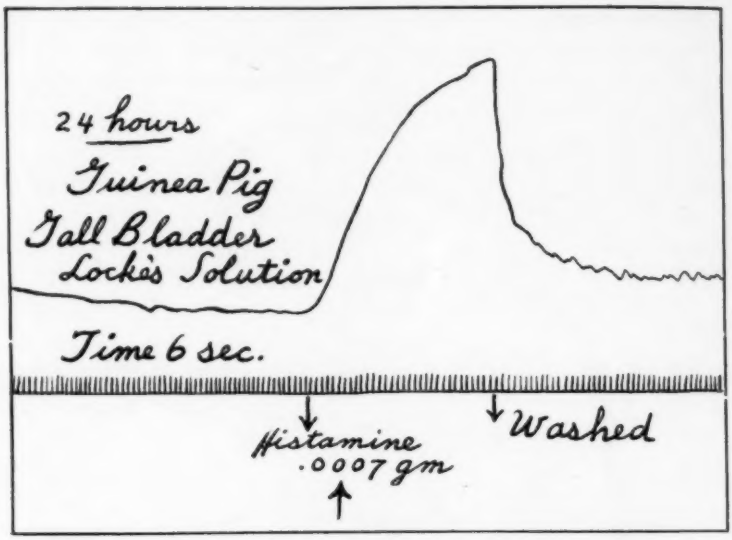

Fig. 15.—Response of the isolated gallbladder of the guinea-pig to histamine. The gallbladder had been isolated twenty-four hours previously.

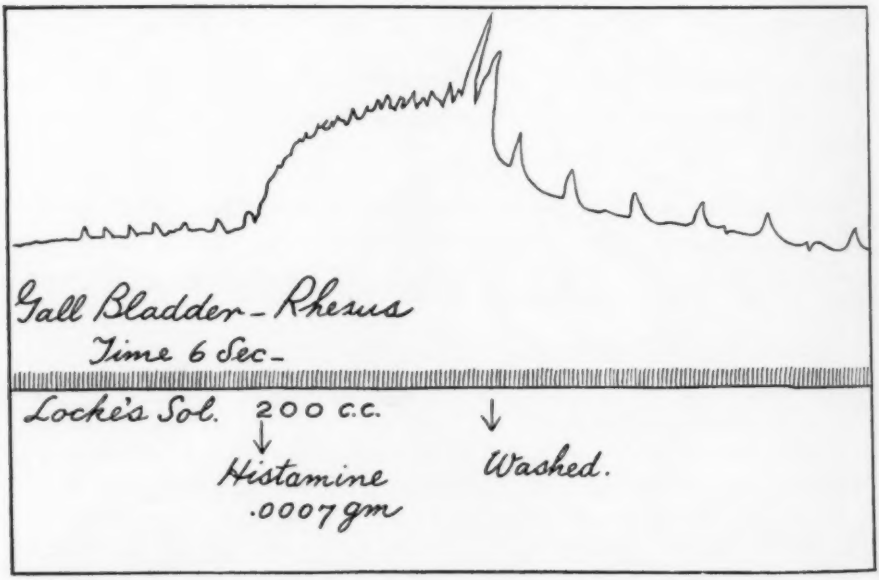

Fig. 16.—Response of the isolated gallbladder of the monkey to histamine.

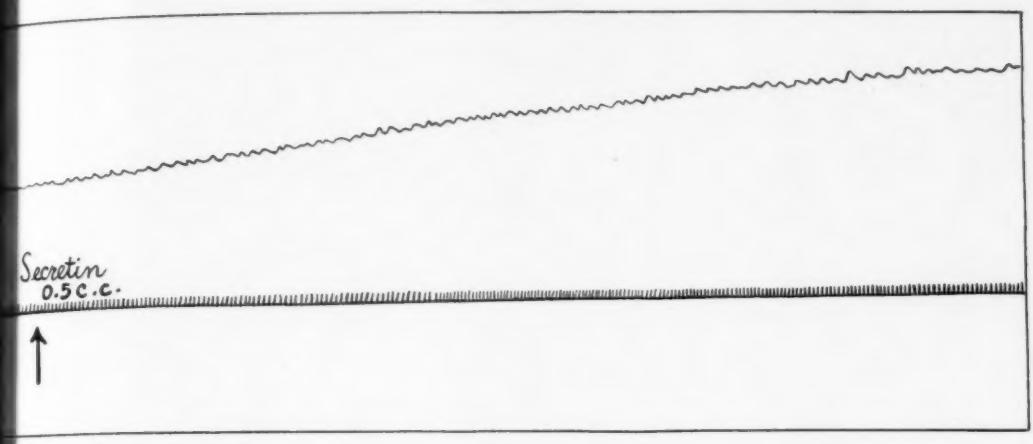

Fig. 17.—Response of the isolated gallbladder of the guinea-pig to secretin.

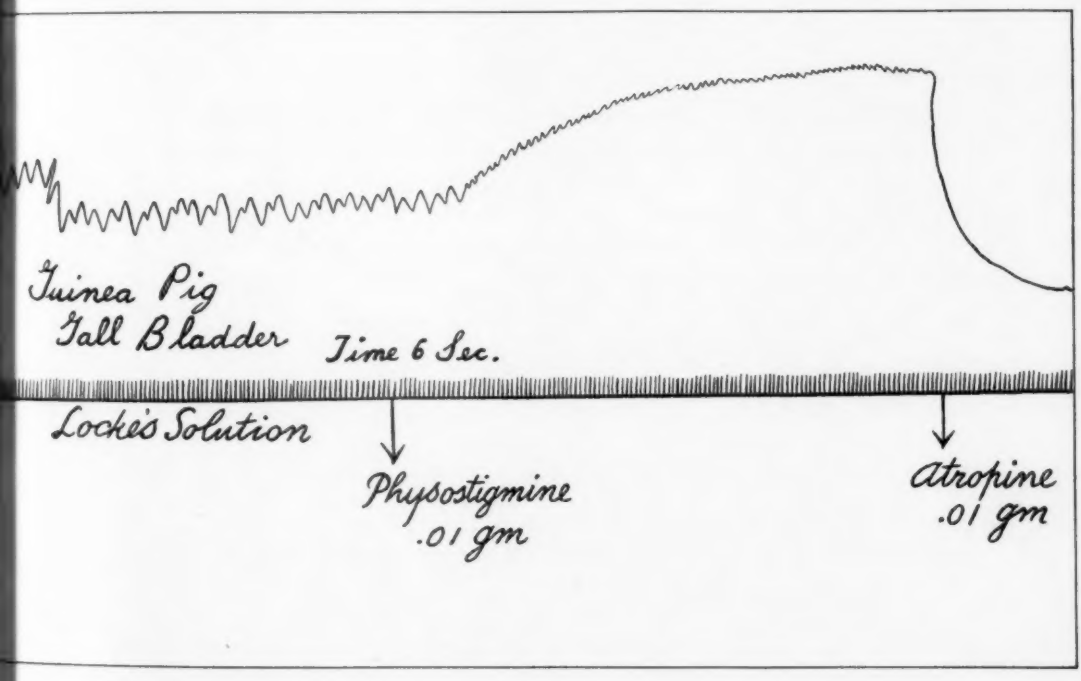

Fig. 18.—Response of the isolated gallbladder of the guinea-pig to physostigmine.

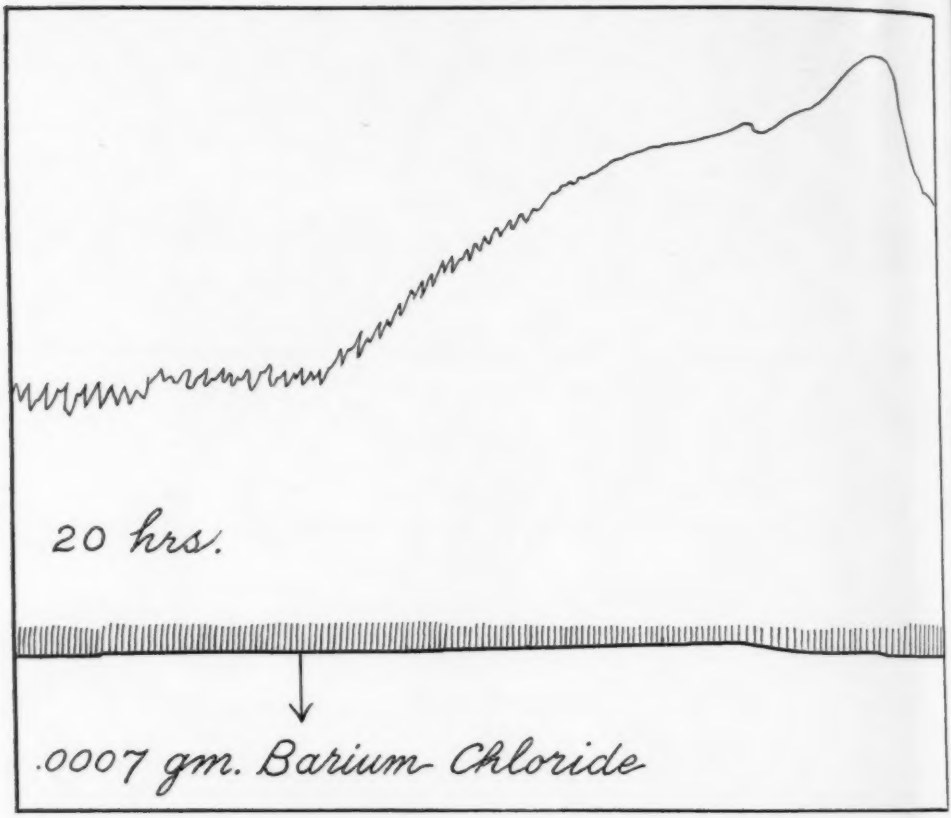

Fig. 19.—Response of the isolated gallbladder of the guinea-pig to barium chloride.

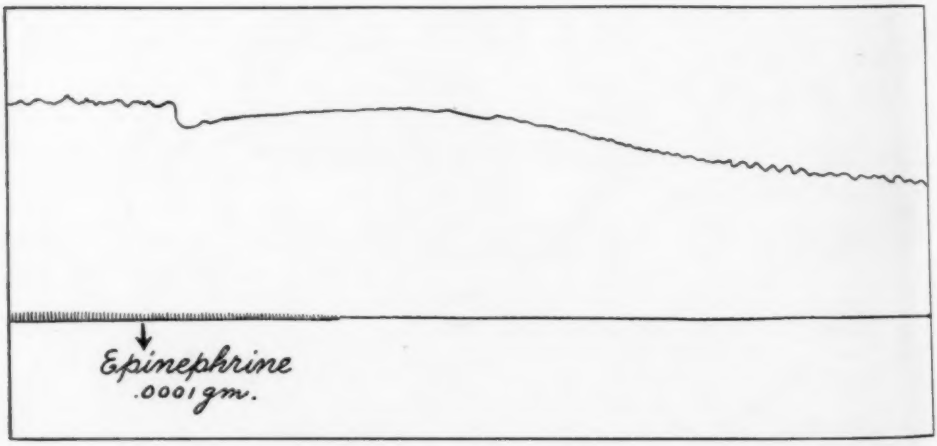

Fig. 20.—Effect of epinephrine on the tonus of the isolated gallbladder of the guinea-pig.

Other Drugs.—Physostigmine also caused contraction of the gallbladder musculature (fig. 18), as did barium chloride (fig. 19). The muscle was paralyzed after the addition of atropine. Contrary to the

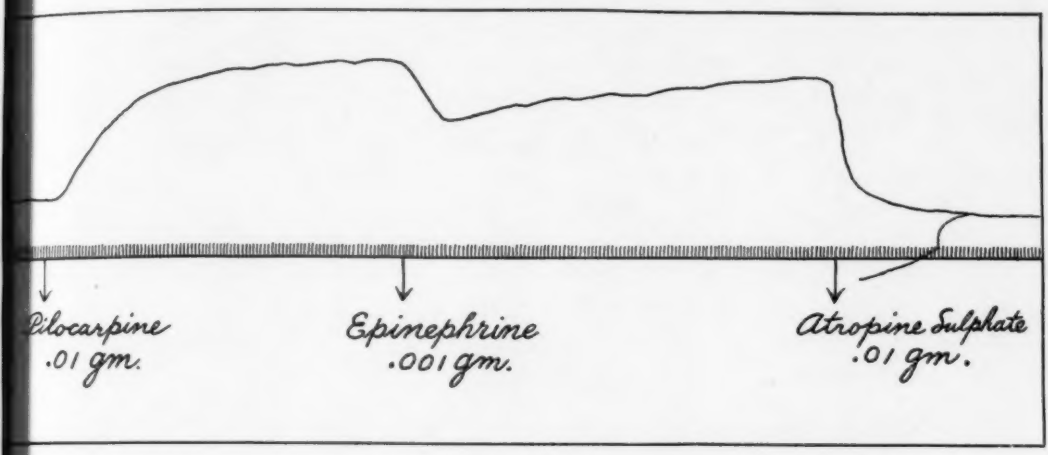

Fig. 21.—The effect of epinephrine on the tonus of the isolated gallbladder of the guinea-pig.

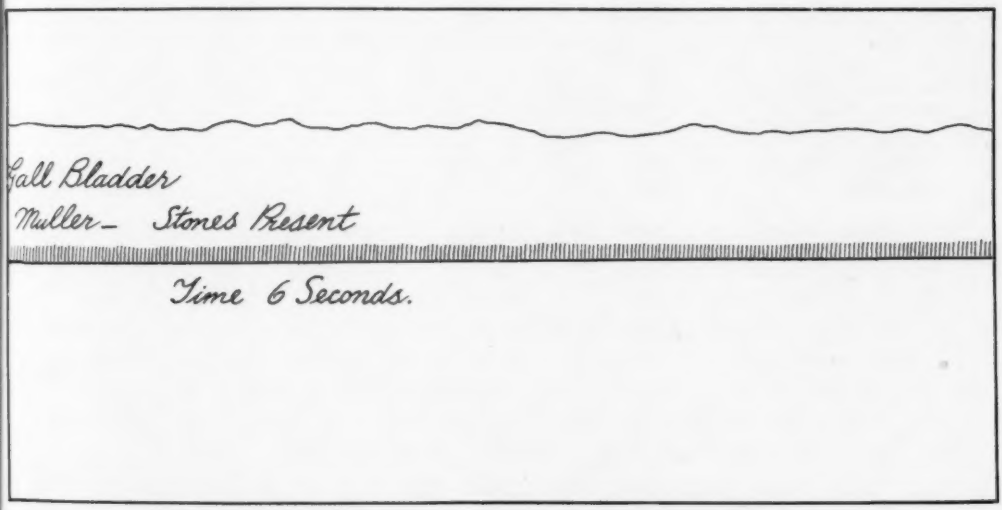

Fig. 22.—Contractions obtained from a diseased human gallbladder without stimulation.

observations of some investigators, we have found that epinephrine causes relaxation of the gallbladder (figs. 20 and 21). In only one experiment of the many that were performed did we observe contraction of the gallbladder following its use.

The Human Gallbladder.—We have not been fortunate enough to obtain a normal human gallbladder for study. That such a gallbladder would respond as do those of the animals we have studied, we cannot question. That even the diseased human gallbladder will show abortive spontaneous contractions is illustrated in figure 22. This gallbladder contained calculi and was the site of chronic interstitial inflammation.

COMMENT

We do not intend to discuss the entire literature on the subject of gallbladder function, which is indeed voluminous, and which was so admirably reviewed by Mann [17] in 1924. Statements are conflicting, and numerous observers have merely repeated older experiments with which they apparently were not familiar. We wish merely to point out a few of the contributions that would tend to confirm the view that we hold that among other functions, some of which may not as yet be known, the gallbladder possesses the ability to contract. With proof of this, it remains for the future to prove whether this mechanism is or is not present for a definite physiologic purpose. The burden of proof rests on those who deny its contractile function.

Freeze,[18] in a paper that seems to have been overlooked by many, found that the gallbladder when stimulated through its motor nerves is capable of contracting against a pressure of at least 220 mm. of Ringer's solution. We obtained figures higher than this for a dog when the cystic duct was connected to a water manometer after the injection of pilocarpine. Our experiment was subject to the error that contiguous structures and vascular effects might have caused a part of the response. Contractions of the magnitude reported by Freeze, while weak when compared to the response obtained from the urinary bladder, nevertheless show a magnitude sufficient to cause bile to leave the gallbladder by way of the cystic duct.

Bainbridge and Dale,[19] in an excellent article published shortly after Freeze published his work, confirmed Doyon's observations of spontaneous rhythmic contractions in the gallbladder. They confirmed the suggestion of Langley, and our data further confirm this, that epinephrine caused relaxation of the gallbladder. They do not agree with Freeze on the exact course of the major motor and inhibitory fibers, but do agree that both sets of fibers are supplied to the gallbladder. Whittaker [7] has obtained contraction of the gallbladder when the nerve supply has been severed. This does not invalidate the previous observations, but demonstrates that the gallbladder can contract inde-

17. Mann, F. C.: Physiol. Rev. **4**:251, 1924.
18. Freeze, J. A.: Bull. Johns Hopkins Hosp. **16**:235, 1905.
19. Bainbridge, F. A., and Dale, H. H.: J. Physiol. **23**:138, 1905.

pendent of its connection with the central nervous system. Bainbridge and Dale believed the increase in tone of the gallbladder in response to pilocarpine to be due to swelling of the liver. This we have shown is not the case, since the isolated gallbladder responds similarly.

In 1915, Lieb and McWhorter [20] studied the action of drugs on strips of the gallbladder by a method similar to that which we have used, and in 1925, Ischiyama [21] reported the results of a study of the isolated gallbladder of the dog in which the gallbladder was intubated through the cystic duct and alterations in pressure recorded with a tambour. The results of these observers are in agreement with our own.

Higgins and Mann [8] stated that "the moot question as to whether the gallbladder ever does empty its contents was definitely settled by Boyden in his studies on cats." Boyden [10] is now convinced that the gallbladder empties its contents through the cystic duct as the result of muscular contraction. The former authors concluded that the gallbladder empties through the cystic duct by the contraction of its own intrinsic musculature, and that other factors are of minor, if of any, importance in this process.

The question as to whether or not respiratory movements are a factor in gallbladder emptying is not as yet definitely settled. Winkelstein and Aschner [11] expressed the belief that the intra-abdominal pressure at the height of inspiration is the major factor in evacuation of the gallbladder. We do not doubt that respiratory movements can cause the evacuation of some bile, but we believe that these are not major factors in the process.

Recently Graham [12] stated that although he was not willing to "ascribe to muscular contractions the exclusive rôle in this drama, . . . perhaps we have not assigned sufficient importance to the factor of intrinsic contractions of the muscle."

Demel and Brummelkamp [4] and Halpert [3] do not deny that some bile leaves the gallbladder by way of the cystic duct, but they deny that the amount is significant. Sweet,[2] on the other hand, definitely stated that what goes in the cystic duct never comes out by this route! In order to prove this, it remains for this group of workers to obtain definite evidence that all the bile constituents leave at a rate consistent with the absorption of water and sodium chloride. Of this we have not been able to obtain confirmatory evidence. This evidence will be published in a series of papers to come from workers in this laboratory. In the blood from the cystic vein of the dog or the lymphatics

20. Lieb, C. C., and McWhorter, J. E.: J. Pharmacol. & Exper. Therap. **7**:83, 1915.

21. Ischiyama, F.: Mitt. a. d. med. Fak. d. k. univ. Kyushu Fukuoka **10**:61, 1925.

of the gallbladder of the cat or dog, we have not found bile pigment in concentrations that could be demonstrated by either the icterus index method of Meulengracht or the diazo method of van den Bergh, even though at the same or subsequent times we obtained evidence that substances such as sodium chloride or sodium iodide pass through the wall of the gallbladder. The pigment must be removed at a rate proportional to the other constituents of the bile or it tends to accumulate, as is evidenced by a comparison of the concentrations of pigment present in liver and in gallbladder bile in the same species. Even though we assumed that there is a threshold for the absorption of bilirubin, judging from the concentration of pigment consistently found in gallbladder bile, we would expect to find the pigment in even greater concentration in the lymph or blood from the gallbladder.

CONCLUSIONS

1. Data are presented which show that, under the conditions of the experiment (isolation), the gallbladder of the dog, guinea-pig and monkey shows rhythmic contractions and responds to stimulation by drugs.

2. We have failed to find certain constituents of the bile in the lymphatics or blood vessels draining the gallbladder.

3. We have observed contractions of the human gallbladder in a patient whose respiration was temporarily checked.

4. From these experiments we are led to conclude that although certain constituents of the bile leave the gallbladder by the lymphatics or blood vessels, concentrated bile leaves the gallbladder by the cystic duct as a result of contraction of the gallbladder.

THE NERVE PATHWAYS IN THE VOMITING OF PERITONITIS*

FRANKLIN E. WALTON, M.D.

ROBERT M. MOORE, M.D.

AND

EVARTS A. GRAHAM, M.D.

ST. LOUIS

A careful review of the literature has failed to disclose any explanation of the mechanism of vomiting in peritonitis which is supported by experimental facts. No recorded attempt by critical experiment to determine the nature of the emetic stimulus and to discover its manner of action could be found, although the phrase "peritoneal irritation" was noted in practically every work on peritonitis and vomiting. The present study was undertaken because of the apparent lack of proof that vomiting in peritonitis is really due to irritation of the peritoneum.

Since the most important subjective evidence on which the interpretation and diagnosis of acute peritoneal inflammation are based consists of the history of abdominal pain, nausea and vomiting, any contribution that leads to a better understanding of the origin and nature of the symptoms is of direct interest to the clinician.

Although the emetic stimulus has usually been considered to be a nervous impulse, it was thought possible that it might be either a hormone or a toxin carried in the blood. Since emesis is induced by the direct application to the vomiting center of minute amounts of certain normal constituents of the blood, such as choline and histamine, it is possible that when one of these is present in the blood in an increased amount, it may cause nausea and vomiting. In intestinal obstruction, which frequently complicates peritonitis, histamine may be present in the blood in abnormally large amounts, and, in such cases, may possibly constitute the stimulus to vomiting.

It is believed that observations recently made in this laboratory tend to exclude the probability of either a toxin or a hormone providing the important emetic stimulus in peritonitis. For example, in a series of fifteen normal cats, intraperitoneal injection of 10 cc. of a 50 per cent turpentine emulsion produced vomiting within six seconds after the injection, a reaction time which seemingly would preclude

* Submitted for publication, June 9, 1930.

* From the Department of Surgery, Washington University School of Medicine and Barnes Hospital.

a chemical stimulation of the center and yet be entirely within the limits of a reflex phenomenon. Furthermore, as will be described shortly, peritonitis failed to produce vomiting in six cats in which the vagus nerves had been divided in the thorax and the abdominal sympathetic and splanchnic innervation destroyed.

If the emetic stimulus is a nervous impulse, the three possible pathways to be considered are the vagi, the sympathetics and those cerebrospinal nerves which also supply the peritoneum, namely, the phrenics, the lower six thoracics, the iliohypogastrics and the ilio-inguinal nerves.

The method of study has been as follows: A twenty-four hour bouillon culture of *B. coli* was injected intraperitoneally into each of twelve normal cats and seven normal dogs, and was found in every instance to produce a fatal peritonitis, the duration of life varying from five to twelve days. Without exception, vomiting was a constant feature of the disease. These animals served as controls.

Twelve other cats that had received similar injections and that had also been subjected to bilateral low intrathoracic vagotomy performed from sixty to seventy-two hours after injection vomited as did the controls and failed to differ in this respect from animals in which the vagi were intact.

Bilateral abdominal sympathectomy and splanchnotomy was performed in five cats. In these animals peritonitis similarly induced by *B. coli* produced vomiting which did not differ in either character or frequency from that seen in the controls.

In five dogs suffering from a colon bacillus peritonitis, the spinal cord was transected at the level of the second thoracic vertebra. Vomiting was feeble thereafter, as the innervation of the abdominal muscles was destroyed, but was definitely present and persistent.

Six cats were first subjected to a bilateral low intrathoracic vagotomy and allowed to recover. Two weeks later, the abdominal sympathetic chains were resected and the splanchnic nerves divided. After one week of convalescence, an intramuscular injection of lobeline sulphate (0.003 mg. per kilogram) was given, and prompt emesis resulted in each instance, demonstrating the integrity of the efferent emetic mechanism. Peritonitis was next induced in these animals by *B. coli*. In this series, a striking result was obtained. Every animal died within six days, and postmortem examination revealed in each instance a frank purulent general peritonitis, the diagnosis being confirmed by microscopic section. Yet not one of the six animals vomited even once during the course of the disease.

PROTOCOL

EXPERIMENT 27 (cat 154).—Dec. 23, 1929: Lobeline sulphate, 0.003 mg. per kilogram of body weight, was injected intramuscularly followed in two minutes by emesis.

December 24: Under intratracheal ether insufflation, the pleural cavity was opened through the tenth interspace (right); the right lung was collapsed and packed away with gauze. The anterior and posterior vagal cords were exposed on the lower part of the esophagus and sectioned. The lung was expanded by obstructing expiration, and the thoracic wall closed in layers. This procedure required fifteen minutes.

December 28: The animal was up and about, eating in apparently normal fashion. Lobeline sulphate, 0.003 mg. per kilogram, was injected intramuscularly followed by prompt emesis.

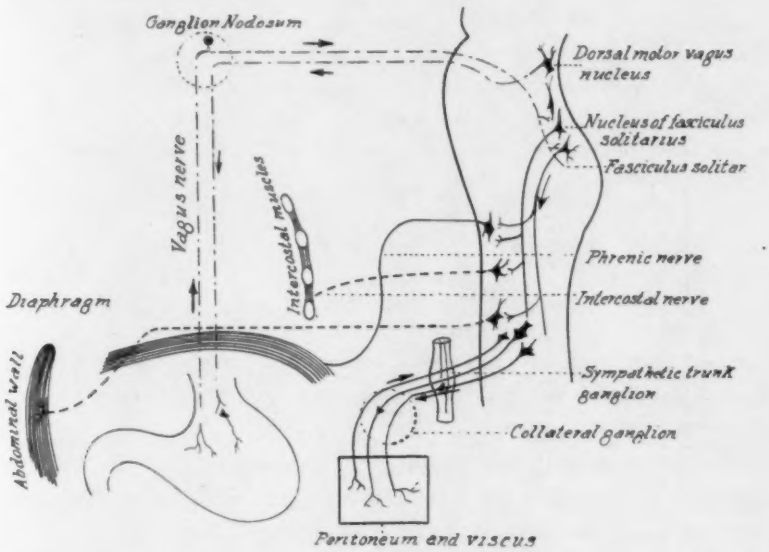

Diagram of the nerve pathways involved in the vomiting produced by peritonitis.

Jan. 3, 1930: Under intratracheal ether insufflation, through a midline abdominal incision, the peritoneal cavity was opened, and the stomach and intestines were brought out and wrapped in warm moist towels. The left major splanchnic nerve was identified at the point of its entrance to the semilunar ganglion and sectioned. The left abdominal sympathetic trunk was identified, followed through the diaphragm and sectioned in the lower part of the thorax, then sesected caudally to the level of the paired ganglions just below the sacral promontory, its minor splanchnic branches being sectioned as exposed. A similar procedure was repeated on the right side. The intestines were replaced, and the abdominal wall was closed in layers.

January 8: The animal was up and about eating in apparently normal fashion. Lobeline sulphate, 0.003 mg. per kilogram, was injected intramuscularly, followed promptly by emesis.

January 9: Twenty cubic centimeters of a twenty-four hour bouillon culture of *B. coli* was injected intraperitoneally.

January 16: The animal died of diffuse, suppurative peritonitis confirmed by autopsy and microscopic examination of tissue. The animal did not vomit during the course of its disease.

Obviously these animals were able to vomit, as demonstrated by the injections of lobeline sulphate. The emetic stimulus was present, as evidenced by all of the animals previously observed. In these animals, then, the emetic action of the peritoneal inflammation had been effectively abolished by the operative procedure, namely, by vagotomy and sympathectomy.

In résumé, in each of forty-six animals in which either the vagus mechanism or the abdominal sympathetic mechanism or both were intact, vomiting was a prominent accompaniment of peritonitis. In each of six animals in which both vagal and sympathetic paths were destroyed, no instance of vomiting was recorded, although the peritonitis was uniformly fatal. It would seem then that colon bacillus peritonitis produced vomiting through a local irritation of afferent nerve endings and not through toxic or humoral changes. The afferent emetic impulse from the peritoneum to the medullary centers evidently traverses only vagal or sympathetic paths, since in the absence of these paths, although cerebrospinal nerves (including the phrenic nerves) are still active, emesis fails to occur. Since the destruction of only one of these paths, i. e., the vagal or the sympathetic, fails to abolish the vomiting of peritonitis, it would appear that the afferent emetic impulse traverses either path with equal facility. This observation is in line with that of Hatcher and Weiss,[1] who found that afferent emetic impulses produced by large oral doses of mercuric chloride ascend over either the vagi or the sympathetics, depending on the integrity of the tract.

COMMENT

From an anatomic and physiologic point of view, there are several factors that apparently enter into the mechanism of vomiting irrespective of the causative one. Some are partially understood and have been confirmed by experimental evidence; others are indefinite and hypothetic. In the foregoing experiments, we have dealt with the vomiting of peritonitis and have found it to be reflex rather than toxic. A brief summary of our knowlege of the nervous mechanism concerned with the vomiting act would perhaps be of interest.

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1. Hatcher, R. A., and Weiss, Soma: Studies on Vomiting, J. Pharmacol. & Exper. Therap. **22**:139, 1924.

Although Giannuzzi [2] was apparently the first to suggest the existence of a vomiting center, Thumas [3] has received the credit for discovering the so-called "center." Forty years ago he described an area lying on both sides of the midline of the floor of the fourth ventricle, the destruction of which with a blunt instrument prevented the emetic action of apomorphine chloride. Much of this older work has been superseded by the careful work of Hatcher and Weiss,[1] who found that the sensory nuclei of the vagus nerves were essential to vomiting in cats. They could not produce emesis after destruction of the sensory nuclei, but they did produce emesis by the application of minute amounts of apomorphine chloride (0.0001 mg.) to the nuclei before destruction. Their explanation of Thumas' failure to produce emesis after destruction of this area is that vomiting cannot be induced when the center is depressed by mutilating operative procedures in its vicinity. In our own laboratory it was found that lobeline sulphate and apomorphine chloride did not produce emesis in either cats or dogs after the floor of the fourth ventricle had been traumatized.

Faradic stimulation of either of the cut ends of the vagus nerves does not regularly induce vomiting. (McCrea, McSwiney and Stopford [4] have recently reviewed the literature in this regard.) Furthermore, Laughton [5] found that while faradic stimulation of the dorsal vagal nucleus of the cat produces contractions of the hypotonic stomach, no emesis resulted. In this connection we have methodically faradized the floor of the fourth ventricle of cats and dogs and have been unable to produce vomiting. Obviously, neither the sensory nucleus of the vagus nerve nor its motor nucleus is per se the vomiting center. However, drugs as employed by Hatcher and Weiss apparently do exert a selective action on certain cells somewhere in the region of the sensory nucleus of the vagus nerve, and thus initiate the sequence of coordinated muscular phenomena that constitute the vomiting act. That faradization has not produced this effect is not necessarily contradictory evidence, for so specific a response may readily fail to appear in the widespread reaction to gross electrical stimulation.

2. Giannuzzi, G.: Untersuchungen über die Organe welche an dem Brechact theilnehmen und über die physiologische Wirkung des Tartarus stibiatus, Centralbl. f. d. med. Wissensch. **3**:1, 1865.

3. Thumas, L. J.: Ueber das Brechcentrum und über die Wirkung einiger pharmakologischer Mittel auf dasselbe, Arch. f. path. Anat. u. Physiol. **123**:44, 1891.

4. McCrea, E. D.; McSwiney, B. A., and Stopford, J. L. B.: The Effect on the Stomach of Section of the Vagus Nerves, Quart. J. Exper. Physiol. **16**:195, 1926.

5. Laughton, N. B.: The Effects on the Stomach of the Stimulation of the Dorsal Vagus Nuclei, Am. J. Physiol. **89**:18, 1929.

Hatcher [6] pointed out the relative importance of a center in the brain to coordinate vomiting. Some species of mammals vomit while others, chiefly the herbivora, do not. The fact that herbivora do not even try to retch under the influence of emetics suggests that they lack a well developed vomiting center.

It is yet a question whether it is actually justifiable to speak of a vomiting center, but as Alvarez [7] aptly put it, "it is certainly convenient to so designate that area in the brain which is essential to the vomiting process in that it receives afferent emetic impulses, discharges efferent ones and coordinates in an orderly sequence the various movements and inhibitions necessary for emesis such as closure of the pylorus, contraction of the lower part of the stomach, relaxation of the fundus, cardia and esophagus, closure of the glottis, stoppage of the respiration, stimulation and inhibition of the diaphragm and stimulation of the abdominal muscles."

Apparently there is some central coordinating mechanism concerned with the vomiting act, since the vomiting induced by an emetic, for example, is indistinguishable objectively from that induced by other causes. The muscles concerned and the efferent nerves do not vary with the causative or afferent impulse, and the discussion of the efferent paths resolves itself into a consideration of the innervation of these muscles.

The diaphragm, which plays an active rôle in vomiting, is supplied by the phrenic nerve. In the embryo, the diaphragm is a derivative of the cervical myotomes that are displaced posteriorly as the diaphragm descends to its permanent level. These myotomes carry down in their descent branches of the third, fourth and fifth cervical nerves. These branches fuse into the phrenic nerve and contain both motor and sensory fibers. It has been reasoned that the motor fibers continue their function in activating the diaphragm, while the sensory fibers, through disuse, may cease to register localized sensations in the diaphragm. However, these afferent fibers retain their ability to carry impulses to the cervical cord as is seen in referred pain in the cervical region following strong stimulation of the central end of a cut phrenic nerve. Although there is indisputable evidence that the sensory fibers do function in the phrenic nerve, work has been presented in this article as evidence that the afferent emetic impulses they carry are negligible if present.

The abdominal muscles, which form the most important group of voluntary muscles, receive their nerve supply from the lower six

6. Hatcher, R. A.: The Mechanism of Vomiting, Physiol. Rev. **4**:479, 1924.

7. Alvarez, W. C.: The Mechanics of the Digestive Tract, ed. 2, New York, Paul B. Hoeber, Inc., 1928.

thoracic, the ilio-inguinal and the iliohypogastric nerves—typical "mixed" cerebrospinal nerves. Although Moritz [8] found that the voluntary muscles of the abdomen in man can exert a pressure on the stomach equal to a column of water 3 meters high, Gold in Hatcher's laboratory caused vomiting in a cat in which the abdominal muscles had been severed longitudinally and transversely so that it was impossible for either them or the diaphragm to compress the stomach. Vomiting in a modified fashion was produced in this laboratory in animals with paralysis of the abdominal muscles. Moreover, one of us recently observed a child of 4 months with congenital absence of the abdominal muscles, who vomited in an apparently normal fashion.

The vagal parasympathetic fibers carry efferent impulses to the stomach and intestines, although the active part these organs play in the vomiting act is secondary. That the stomach is not essential for the vomiting act was probably first demonstrated by Magendie's [9] classic experiment in which he replaced a dog's stomach with a pig's bladder and produced vomiting. Even more striking, however, is the work of Eggleston and Hatcher,[10] who saw typical movements with the expulsion of a considerable volume of frothy mucus from the esophagus following the extirpation of the stomach and intestines with the cardia tied. Rost [11] stated that men and women often vomit after total gastrectomy.

The sympathetic fibers presumably carry efferent emetic impulses. However, this pathway would appear relatively unimportant in the light of experiments which have been detailed, for it was found that after section of the splanchnics and abdominal sympathectomy, the efferent emetic mechanism in cats was apparently not disturbed, as every animal vomited after the intramuscular injection of lobeline sulphate. Similarly, Hatcher and Weiss [12] observed that the emetic action of a peripheral emetic such as mercuric chloride was not inhibited when the spinal cord was sectioned at the level of the second thoracic vertebra. Results paralleling these were obtained by us in dogs with peritonitis which vomited although the spinal cord had been severed at the same level.

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8. Moritz: Studien über die motorische Thätigkeit des Magens: I. Mitteilung ueber das Verhalten des Druckes im Magen, Ztschr. f. Biol. **32**:313, 1895.

9. Magendie: Mémoire sur le vomissement, 1813, quoted by Hatcher (footnote 6).

10. Eggleston, C., and Hatcher, R. A.: The Seat of the Emetic Action of Apomorphine, J. Pharmacol. & Exper. Therap. **3**:551, 1912.

11. Rost, F.: The Pathologic Physiology of Surgical Diseases, trans. by S. P. Reimann, Philadelphia, P. Blakiston's Son & Company, 1923.

12. Hatcher, R. A., and Weiss, Soma: The Seat of the Emetic Action of the Digitalis Bodies, Arch. Int. Med. **29**:690 (May) 1922.

As regards the parasympathetics, Hatcher and Weiss found that after a large oral dose of mercuric chloride, section of the vagi in the neck failed to inhibit emesis. In like manner, in our experience the vomiting of cats and dogs was not affected by intrathoracic section of the vagi.

Exner and Schwarzmann [13] reported twenty cases of gastric crises in which there apparently was no abnormality in the vomiting mechanism following bilateral vagotomy. Latarjet, Schiossi and Mayo [14] have performed similar neurectomies without disturbing the vomiting mechanism.

That the efferent impulse is a nervous impulse has been shown by the fact that transection of the cord at the level of the second thoracic vertebra and bilateral vagotomy in the same animal followed by the injection of apomorphine chloride evoke practically no retching response in the dog, although the diaphragm can be felt to contract in a normal fashion.

The possible anatomic pathways for afferent impulses arising from peritoneal irritation include the lower six thoracic nerves, the ilio-inguinal, the iliohypogastric, the phrenic and the vagus nerves and the general visceral afferent fibers which traverse the sympathetic trunks. The peritoneum lining the abdominal wall receives its innervation from the seventh to the twelfth thoracic, the ilio-inguinal and the ilio-hypogastric nerves, which are cerebrospinal mixed nerves. The peritoneal surface of the diaphragm likewise receives some fibers from these intercostal nerves and also from the ramifications of the phrenic nerve, which is in reality a "displaced" branch of the cervical plexus and a cerebrospinal mixed nerve. Thus, the sensory nerve supply of the entire parietal peritoneum is derived from somatic elements. The visceral peritoneum, on the contrary, is supplied by the vagus and sympathetic nerve trunks, which contain afferent fibers belonging to the visceral rather than to the somatic group. This distinction seems to be significant in view of the results of experiments performed in our laboratory. Differential denervation of the peritoneal surfaces, as previously detailed, indicates that there are only two afferent pathways for emetic impulses in peritonitis, namely, the vagal and sympathetic trunks. In animals with the phrenic and other cerebrospinal

13. Exner, A., and Schwarzmann, E.: Gastrische Krisen und Vagotomie, Mitt. a. d. Grenzgeb. d. Med. u. Chir. **28**:15, 1914.

14. Latarjet, A.: Resection des nerfs de l'estomac: Technique opératoire, résultats cliniques, Bull. Acad. de méd. **137**:681, 1922. Schiossi, B.: The Rôle of the Pyloro-Duodenal Nerve Supply in the Surgery of Duodenal Ulcer, Ann. Surg. **81**:939, 1925. Mayo, C. H.: Division of the Vagi for Pylorospasm, Ann. Surg. **88**:669, 1928.

nerves intact subjected to a bilateral abdominal sympathectomy, splanchnotomy and bilateral intrathoracic vagotomy, peritonitis did not cause vomiting. Since in these animals the innervation of the parietal peritoneum was still intact, it seems reasonable to conclude that only the visceral afferent fibers are of importance in the reflex vomiting act, and that it is irritation of the visceral rather than of the parietal peritoneum that causes vomiting in peritonitis.

The apparent localization of the afferent emetic pathways in the vagus and sympathetic nerves and the exclusion of the cerebrospinal nerves from such a system are rather striking in the light of clinical observation as expressed by Weiss and Davis.[15] "That the relief of pain is due to blocking of cutaneous afferent impulses and that the infiltration with novocain does not exert an indirect influence on the visceral afferent sympathetic impulses is shown by observations on patients who aside from visceral pain also suffer from nausea and vomiting due to the same cause as the pain." In these patients the skin infiltration abolished pain at once, but the vomiting persisted. The persistence of vomiting after blocking of the pain fibers (cerebrospinal) indicates that strong visceral afferent impulses continue to reach the high centers through the sympathetic and vagal chains.

SUMMARY

The experiments here reported show that the vomiting of peritonitis is the result of the stimulation of afferent nerve endings located in the peritoneum.

The emetic impulse thus initiated passes to the medullary center by way of sensory nerve fibers which are included in both the vagal and sympathetic trunks. Section of these trunks prevents the occurrence of vomiting in peritonitis, although phrenic and other cerebrospinal nerve paths are left undisturbed.

Since by sympathectomy alone or by vagotomy alone vomiting in peritonitis is not abolished, the afferent emetic impulse evidently traverses either pathway with equal facility.

The consensus among anatomists seems to be to the effect that the parietal peritoneum is chiefly supplied by cerebrospinal somatic afferent nerves, whereas the visceral peritoneum receives its supply from the visceral afferent fibers that course in the vagal and sympathetic trunks. If this point of view is correct, the foregoing experiments indicate that it is the irritation of the visceral and not of the parietal peritoneum that gives origin to the vomiting in peritonitis.

15. Weiss, Soma, and Davis, David: The Significance of the Afferent Impulse from the Skin in the Mechanism of Visceral Pain, Am. J. M. Sc. **176**:517, 1928.

PANCREATIC CYSTS

REPORT OF FORTY-SEVEN CASES *

E. STARR JUDD, M.D.
HAMLIN MATTSON, M.D.
Fellow in Surgery, the Mayo Foundation
AND
HOWARD R. MAHORNER, M.D.
Fellow in Surgery, the Mayo Foundation
ROCHESTER, MINN.

Few clinical studies of large series of cysts of the pancreas have been reported in the literature, and only brief attention has been paid to the pathologic changes of this disease. Of 723,397 patients admitted at the Mayo Clinic, eighty-eight with cyst of the pancreas have been operated on. One of us,[1] in 1921, reported forty-one cases from the clinic, the largest original series recorded up to that time. This paper includes a review of the literature and a clinical survey, with comment, of the forty-seven patients treated surgically at the clinic since the report in 1921. A study of the etiology and pathology of this disease will be presented elsewhere.

Morgagni,[2] in 1761, described multiple cysts on the pancreas, mesentery and omentum in a cadaver. Claessen,[3] in 1842, reviewed a series of cases from the literature. "The treatment (of cysts of the pancreas) must be of the symptoms as they arise and by diet," wrote Friedreich,[4] in 1875, in the first basic monograph on the subject. As early as 1862, Le Dentu [5] punctured a cyst of the pancreas and drained it, in the belief that it was a cyst of the liver. Peritonitis developed, and the patient died. "Cysts of the pancreas," he wrote, after this experience, "should be relegated to the list of those affections where the healing art is impotent."

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* From Division of Surgery, the Mayo Clinic.

1. Judd, E. S.: Cysts of the Pancreas, Minnesota Med. **4**:75 (Feb.) 1921.

2. Morgagni, G. B.: The Seats and Causes of Diseases, London, A. Millar and T. Codell, and Johnson and Payne, 1909, vol. 5, p. 578.

3. Claessen, H. J.: Die Krankheiten der Bauchspeichdeldrüse, Köln, M. Du Mont-Schauberg, 1842, pp. 368.

4. Friedreich, N.: Cysts of the Pancreas, in von Ziemssen, H.: Cyclopaedia of the Practice of Medicine, New York, William Wood & Company, 1878, vol. 8, p. 615.

5. Le Dentu, M.: Rapport sur l'observation précédente, Bull. Soc. anat. de Paris **10**:197 (March) 1865.

Lücke,[6] in 1866, drained a cyst of the pancreas; the patient died. Bozeman,[7] in 1881, extirpated a cyst successfully. The next year, Gussenbauer,[8] a pupil of Billroth, made a tentative diagnosis of cyst of the pancreas before operation and devised a method of drainage whereby he sewed the parietal peritoneum to the skin, and the walls of the cyst to the parietal peritoneum. Marsupialization became, and has remained, a standard surgical procedure.

There followed detailed studies of individual cases of cyst by Fenger,[9] W. J. Mayo,[10] Osler,[11] McBurney,[12] Senn,[13] and others. Experimental work was done by Senn [14] and Thiroloix.[15] Such studies were reviewed in monographs by Körte,[16] Lazarus,[17] and Oser,[18] and much of our present knowledge is based on them.

The body of the pancreas lies behind the stomach. It is on a level with the first lumbar vertebra and on the boundary between the peritoneal and retroperitoneal spaces. The cyst makes its way toward the anterior parietal peritoneum in the line of least resistance. Hence, its

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6. Lücke, A., and Klebs, E.: Beitrag zur Ovariotomie und zur Kenntnis der Abdominalgeschwülste, Virchows Arch. f. path. Anat. **41**:1 (Nov.) 1867.

7. Bozeman, N.: Removal of Cyst of Pancreas Weighing Twenty and One-Half Pounds, M. Rec. **21**:46 (Jan. 14) 1882.

8. Gussenbauer, Carl: Zur operativen Behandlung der Pankreascysten., Arch. f. klin. Chir. **29**:355, 1883.

9. Fenger, Christian: A Case of Traumatic Cyst of the Pancreas, Chicago M. J. & Exam. **66**:74, 1888.

10. Mayo, W. J.: Pancreatic Cyst: Uretero-Vaginal Fistula, the Result of Vaginal Hysterectomy: Successful Reimplantation of Ureter into the Bladder, M. Rec. **45**:168 (Feb. 10) 1894.

11. Osler, William: Lectures on the Diagnosis of Abdominal Tumors: Lecture V. Tumors of the Intestine, Omentum and Pancreas; Miscellaneous Tumors, New York M. J. **59**:545 (May 5) 1894.

12. McBurney, Charles: Cyst of the Pancreas, Ann. Surg. **19**:492, 1894.

13. Senn, Nicholas: The Surgical Treatment of Cysts of the Pancreas, Am. J. M. Sc. **90**:17 (July) 1885; The Surgery of the Pancreas, As Based Upon Experiments and Clinical Researches, ibid. **93**:121 (Jan.) 1887; Experimental Surgery, Chicago, W. J. Keener, 1889, p. 379.

14. Senn, Nicholas: The Surgery of the Pancreas, as Based on Experiments and Clinical Researches, Am. J. M. Sc. **92**:141 (July) 1886.

15. Thiroloix, J., quoted by Oser (footnote 18).

16. Körte, W.: Die chirurgischen Krankheiten und die Verletzungen des Pankreas, Deutsche Chirurgie, Stuttgart, Ferdinand Enke, 1898, pp. 234.

17. Lazarus, Paul: Beitrag zur Pathologie und Therapie der Pankreaserkrankungen mit besonderer Berücksichtigung der Cysten und Steine, Ztschr. f. klin. Med. **51**:203, 1904.

18. Oser, Leopold: Diseases of the Pancreas; in Nothnagel: Encyclopedia of Practical Medicine: Diseases of the Liver, Pancreas and Suprarenal Capsules, Philadelphia, W. B. Saunders Company, 1903, p. 180.

ultimate relations are influenced by the point of origin in the gland, the reflection of the peritoneum, and the arrangement of the overlying viscera. Most frequently, the cyst presses into the lesser peritoneal cavity and presents between the stomach and the transverse colon, and behind the gastrocolic omentum (fig. 1). The next most common site

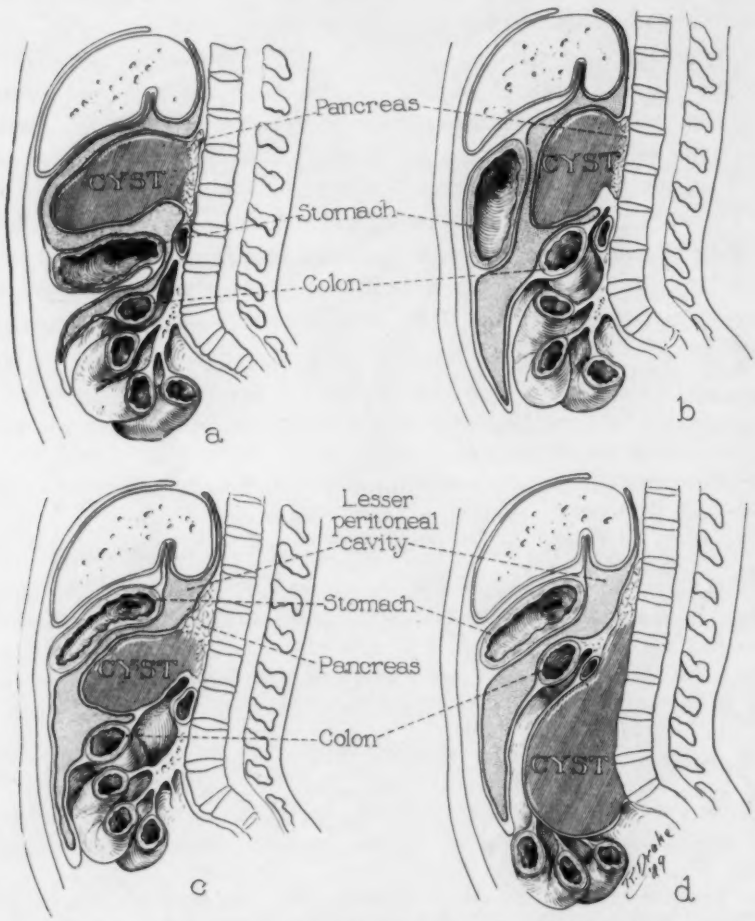

Fig. 1.—The relations of cyst of the pancreas to abdominal viscera. The most common site is exemplified in *c*; next in frequency are the situations shown respectively in *a* and *b*. The situation shown in *d* is very infrequent.

is between the stomach and the liver or protruding into the lesser peritoneal cavity behind the stomach (fig. 1 *a* and *b*). However, the cyst may invaginate itself between the layers of the mesocolon, and when it does this, it usually presents behind the transverse colon. Anatomi-

cally, the layers of the transverse mesocolon separate along the pancreas and cover its anterior surface. The cyst will rarely cause bulging of the inferior surface of the transverse mesocolon, downward and forward, and so will lie below the colon, as in the cases reported by Hersche [19] and others. In one of the cases in our series, the cyst was found in the pelvis, between the layers of the mesocolon of the sigmoid. Martin [20] reported finding a cyst of the pancreas directly behind the descending colon. The cyst may burrow toward the pelvis, wholly retroperitoneally, as in the case reported by Hulke.[21] A cyst reported by Primrose [22] had burrowed behind the posterior parietal peritoneum.

Most important in the recognition of cysts of the pancreas are the character and situation of the mass. A smooth, relatively immobile hemispheric swelling, with tense walls, is characteristic. In most of the cases, such a swelling is in the upper part of the abdomen, between the ensiform cartilage and the umbilicus, in the median line or to the left of it. In forty-five of the forty-seven cases, more than 95 per cent, a tumor was felt above the umbilicus. In twenty-one cases, it was to the left of the median line, in eleven, approximately in the median line, and in thirteen, to the right of the median line. In one case, the tumor was felt in the pelvis and was found to be enclosed in the mesentery of the sigmoid. A mass was felt in one hundred and fourteen of Körte's one hundred and twenty-one cases which were reviewed from the literature; in forty-eight cases the mass was in the median line; in forty, it was situated to the left, and in ten it was situated to the right of the median line; in sixteen cases, the mass appeared below the level of the umbilicus.

Cyst of the pancreas, as a rule, is relatively immobile. When it is situated in the tail of the gland, and without adhesions, it may be freely movable. Mobility was noted in eleven of the cysts in our series. Nine of the mobile cysts were found to originate in the tail of the gland. In two cases, the point of origin was not given. Respiratory movements will be felt when the cyst is in contact with the diaphragm, or when pressure is transmitted from the diaphragm. Five cysts were noted as moving with respirations. Of this number, two

19. Hersche, J.: Operation einer Pankreascyste von seltener anatomischer Lagerung, Wien. klin. Wchnschr. **5**:727 (Dec. 22) 1892.

20. Martin, A.: Ein Fall von Pankreascyste, Virchows Arch. f. path. Anat. **120**:230 (May) 1890.

21. Hulke: Pancreatic Cyst, in Reports of the Clinical Society of London, Lancet **2**:1273 (Dec. 3) 1892.

22. Primrose, A.: Pancreatic Cysts and Pseudocysts: Report of a Case of Total Extirpation by an Extraperitoneal Method, Surg. Gynec. Obst. **34**:431 (April) 1922.

were found next to the liver and two were very large. The percussion note is deadened where the tumor is most prominent; in the periphery, an intestinal percussion note can be demonstrated. A zone of tympanitic percussion usually is found between the cyst and the liver. Palpation and percussion in various positions of the body will help to clarify the relation of the mass to abdominal organs.

The appearance of the mass is the most important objective symptom. Twenty-four of the forty-seven patients complained of a mass in the abdomen. Three of this number described it as fulness. In the majority of cases, the mass developed gradually. However, in one instance it was noticed three days, and in another six days, after an accident. One patient said the mass appeared over night. Another patient complained of a feeling of pressure in the epigastrium, but only when the stomach was filled with food. Payr [23] cited a case in which the tumor disappeared and recurred three times in two months. The cyst described by Hersche fluctuated in size. Two of the patients in our series gave a history of disappearance of the mass. In one of the two, a cystadenocarcinoma was found.

Pain is the most important of the subjective symptoms of cyst of the pancreas. Forty-three of the forty-seven patients (91 per cent) complained of pain. Studies concerning the incidence of pain in patients who have only cyst of the pancreas are not available in the literature. Disease was found in other organs in nineteen cases in our series. In thirteen cases, choleliths were present, and in three, gross evidence of cholecystitis only was found. More than 34 per cent, therefore, gave evidence of cholecystitis, as compared to 41 per cent of the series reported by Judd in 1921. Gross evidence of pancreatitis was found in four cases, in one of which pancreatic stones were present. In one case, the pancreatitis was found together with cholelithiasis. Pancreatitis was found with duodenal ulcer and appendicitis in another case. Necrosis of abdominal fat was found in one case of pancreatitis. In twenty-eight cases, only cyst of the pancreas was found; twenty-four of these patients, more than 85 per cent, complained of pain. The four cases classed as malignant and probably malignant were in this group. In thirteen cases, the pain was in acute attacks. In eleven cases, the pain was more or less steady. Four patients with cyst only did not complain of pain, although two in this group said they had indefinite abdominal distress. A malignant cyst was found in one of the four cases.

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23. Payr, Erwin: Pankreascyste, seltene Topographie, Operation und Heilung, Wien. klin. Wchnschr. **11**:629 (June 30) 1898.

Cholecystitis and pancreatitis are frequently associated with cyst of the pancreas and must be considered in evaluating the symptoms of this disease. Organs in the upper part of the abdomen are in intimate association. The frequency of cholecystic disease in cyst of the pancreas indicates that cysts of the pancreas, following inflammatory manifestations in the upper part of the abdomen, probably are only obvious residual signs of a process which has involved not only the pancreas, but adjacent organs as well.

Of the associated symptoms, influence on the general health, jaundice and nausea and vomiting are significant. The general health was affected severely in most of the cases in our series. Loss of weight and weakness were two of the most common symptoms. In nineteen of the forty-three patients who had unquestioned benign cyst, there was no loss of weight. In twenty-nine of the total number of forty-seven cases, the losses ranged from 4 to 60 pounds (1.8 to 27.2 Kg.). Seventeen patients lost less than 25 pounds (11.3 Kg.), and twelve lost more than 25 pounds (11.3 Kg.). Of the two patients with malignant cysts, one lost 10 pounds (4.5 Kg.) in three months and the other lost 17 pounds (7.7 Kg.) in a year. Of the two patients with cysts which were probably malignant, one lost 10 pounds (4.5 Kg.) in two weeks and the other lost 20 pounds (9.0 Kg.) in four months. Nausea and vomiting were common complaints.

In ten cases there was a definite history of jaundice. In three other cases, the history of jaundice was doubtful. Of the thirteen cases, cholecystitis with stones was present in three, and a thickened gallbladder in two. Jaundice was said to be caused by pressure of the cyst on the common bile duct in nine of one hundred and twenty-one cases which were reviewed by Körte. Excess fat in the stools was found in only two cases in our series. In one case, stones were present in the duct of Wirsung, and in the other case the wall of the gallbladder was thick. In three cases there was a history of diarrhea. Evidence of cholecystitis was found in two of the three cases and there was a history of jaundice in one of the two. In three cases, the patients gave a history of having passed clay-colored stools. In one case, only a cyst was found. In one case of cyst of the pancreas and chronic cholecystitis with stones, the patient had had spells during which tarry stools were passed. In eighteen cases the patients complained of constipation. Unilateral hematuria in a case reported by Ransohoff [24] was found to be due to pressure of the pancreatic cyst on the left renal vein.

24. Ransohoff, Joseph: Pancreatic Cyst as a Cause of Unilateral Hematuria, with Report of a Case, Tr. South. Surg. & Gynec. A. **28**:119, 1915.

The interval between onset of first symptoms and the patient's admission in our series varied from two weeks to twenty years. Five patients gave a history of symptoms extending over a month or less. Twenty-five of the forty-seven patients, more than 53 per cent, gave a history of less than twelve months' duration. Hulke saw a patient who apparently had had a cyst for forty years. Sensations of epigastric distress, weight and fulness early in the disease were complained of.

There were twenty-eight women and nineteen men in our series. The age distribution is shown in the tabulation. In Körte's one hundred and twenty-one cases reviewed from the literature, there were sixty men and fifty-six women. Sex was not specified in five cases. Thirty-six cases occurred in the fourth decade and thirty in the third decade. Of the patients who had benign cysts in our series, the youngest was 20 and the oldest 72 years of age. Railton [25] reported a case in an infant aged 6 months. Two of the forty-seven cysts were proved to be malig-

Age Distribution by Decades of Patients With Cyst of the Pancreas

Decade	Cases	Benign	Malignant	Probably Malignant
Third	11	11	..	..
Fourth	9	7	2	..
Fifth	12	12	..	..
Sixth	9	9	..	..
Seventh	5	3	..	2
Eighth	1	1	..	..
Total	47	43	2	2

nant at necropsy. Two were classified only as probably malignant because microscopic confirmation was lacking.

With a rapidly rising tumor of the epigastrium following acute inflammatory conditions, cyst of the pancreas becomes a probability. Cyst of the ovary, mesenteric and omental cyst, cyst of the liver, hydrops of the gallbladder, cyst of the suprarenal capsule, fluid tumor of the kidney, retroperitoneal tumors, cyst of the posterior gastric wall, cyst of the spleen, and aneurysm, may have to be considered in differentiation. Large cysts of the pancreas are reported in the literature as being mistaken frequently for ovarian cyst. The uterus is in its normal position, usually, when cyst of the pancreas is present, and it is possible to palpate the ovary in most cases; in cases of large ovarian cyst, the uterus is more likely to be pushed to the side of the pelvis. The patient may aid the differentiation of ovarian and pancreatic cyst by relating that the mass grew from above downward or from below upward.

25. Railton, T. C.: A Case of Pancreatic Cyst in an Infant, Brit. M. J. **2**:1318 (Oct. 31) 1896.

Moynihan [26] stated that mesenteric cysts are characterized by prominence of the tumor near the umbilicus, great mobility, especially transversely, possibility of rotation about a central axis, and the presence of a belt of resonance across the cyst. A cyst of the omentum usually is very mobile. However, if it arises directly below the greater curvature of the stomach, such a cyst may give signs and symptoms identical with cyst of the pancreas.

Hydatid cyst of the liver may cause hemispheric bulging in the epigastrium. A band of resonance separates a pancreatic cyst from the liver in typical cases and aids in differentiation. In giant hydrops of the gallbladder, the dulness of the tumor and of the liver is nearly always continuous. The hydrops will have axial mobility unless restrained by adhesions. Suprarenal cysts are less common than cysts of the pancreas; Moynihan stated that they enlarge most commonly above the transverse mesocolon. However, they may grow between the layers of the transverse mesocolon. Obviously, distinction from cysts of the pancreas is impossible with such relations.

Fluid tumors of the kidney, such as hydronephrosis, cysts and pyonephrosis, usually are ruled out by the history and urograms. Retroperitoneal sarcomas may present similarity to cysts of the pancreas, but are nonfluctuant unless cystically degenerated. Retroperitoneal cysts and cysts of the posterior gastric wall may take the same line of growth as cysts of the pancreas, and distinction is hardly possible. An area of resonance usually separates cyst of the pancreas from the spleen, and distinguishes it from splenic cyst. A cyst of the pancreas which lies over the aorta may be confused with aneurysm. Expansile pulsation is absent in a cyst. Abscesses of the pancreas arise rapidly and are more sensitive to pressure than cysts. Total necrosis gives rise to much more severe symptoms. In summary, differential diagnosis may be restricted to ovarian, mesenteric, omental, splenic and hepatic cysts, hydrops of the gallbladder, fluid tumors of the kidney, retroperitoneal sarcomas and aortic aneurysm. Suprarenal and retroperitoneal cysts and cysts of the posterior gastric wall are indistinguishable from cysts of the pancreas, but are extremely rare.

Roentgen examination is a major aid in the diagnosis of cysts of the pancreas. A filling defect in the stomach, which can be eliminated by displacing the stomach, or displacement of the duodenum and small intestines, points toward the diagnosis of cyst of the pancreas. An enlarged duodenal curve is characteristic of enlargement in the region of the head of the pancreas. Small cysts may be confused roentgenologically with benign tumors of the stomach. The stomach and colon

26. Moynihan, B. G. A.: Mesenteric Cysts, Ann. Surg. **26**:1 (July) 1897.

have been dilated as an aid in diagnosis. Gussenbauer called attention to this, and the method was used commonly before the advent of roentgen rays. Diagnostic aspiration is dangerous and is of historic interest only. The presence of a ferment in the cystic fluid is not diagnostic, for other fluids, such as ascitic fluid, the contents of ovarian cyst, and pleural exudates, have been found to contain starch-splitting ferments. In many cysts of the pancreas, ferments are not to be found.

Cyst probably was the first disease of the pancreas to be treated surgically. Choice of operation depends on the size, variety, situation and condition of the cyst. The ideal treatment is complete removal, if possible, because by such a procedure the inconvenience of prolonged drainage is obviated. In the clinic the removal was not attempted except in carefully selected cases. With such precautions there was little difference as to the risk and the ultimate outcome between removal and drainage. A small cyst with few adhesions situated preferably in the tail of the pancreas with narrow pedicle usually should be extirpated. In cases in which the cyst is large and adherent and in which the glandular tissue encroaches considerably on the cyst, marsupialization is the method of choice.

Seven of the forty-seven cysts in this series were excised completely. Most of these cysts measured from 6 to 10 cm. in diameter. One cyst of a diameter of 20 cm. was removed. Thirty-three of the cysts were marsupialized and drained in one stage. The cyst is drained by a puncture with a needle, and the aperture is clamped. The peritoneum covering the cyst, and the parietal peritoneum, are sutured; the cyst is opened, and a rubber catheter and sometimes iodoform gauze are introduced. In some cases the cyst was packed. Sometimes a purse string suture was applied about the drainage tube. Total excision was carried out in seven cases, in all of which the cysts were benign. Partial excision and drainage was done in six cases. Exploration only was done in one case, in which the cyst was malignant. Epithelial lining usually is absent from the cyst. Judd advocated destroying such a membrane mechanically, when one is present. Schwyzer [27] applied tincture of iodine to the interior of the cyst. Primrose sewed the posterior parietal peritoneum to the anterior parietal peritoneum before opening the cyst. Other procedures that have been used for cyst of the pancreas are aspiration, partial extirpation, anastomosis with the gallbladder, anastomosis with the jejunum and puncture of the cyst with subsequent roentgen treatment. Schwyzer used the extraperitoneal approach through a lumbar incision. Peters [28] exposed a

27. Schwyzer, Arnold: Discussion, Minnesota Med. **4**:82 (Feb.) 1921.

28. Peters, G. A.: Hydatid Cyst of the Tail of the Pancreas, Canad. Pract. & Rev. **26**:75, 1901.

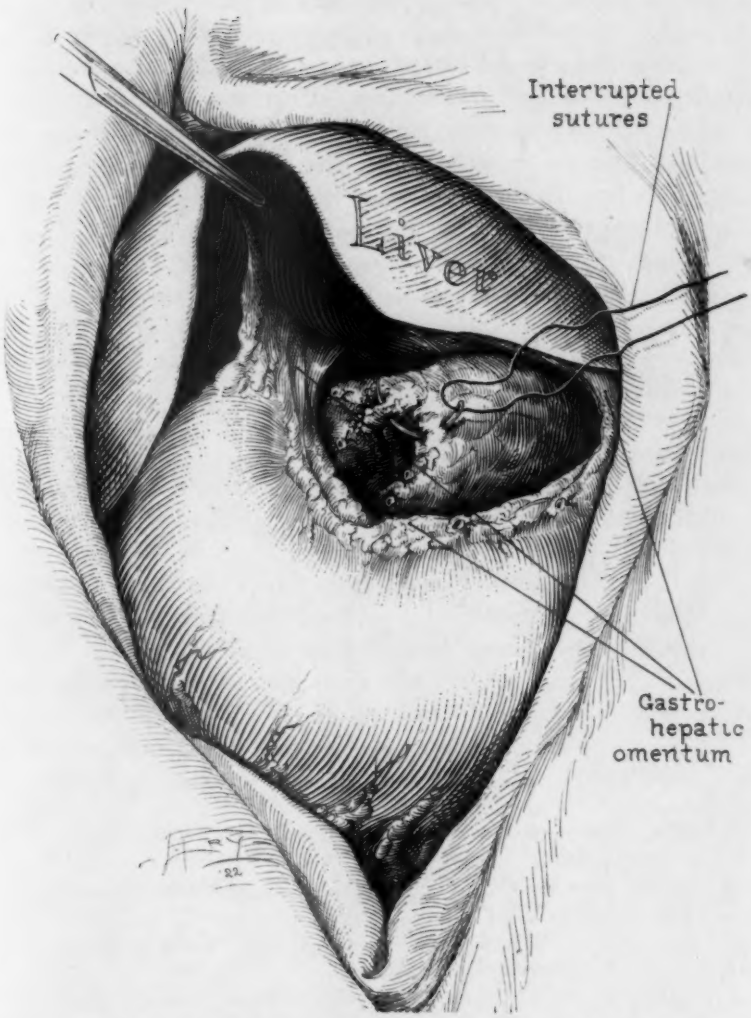

Fig. 2.—The first step in technic after resection of cyst.

cyst in the tail of the pancreas by a left lumbar incision parallel to the last rib. Willis [29] excised a cyst which was adherent to the aorta and Kosiński [30] is said to have divided the pedicle of a cyst by cautery.

Dangers of allowing a cyst to remain, aside from the inconvenience to the patient, are probability of enlargement, threat of mechanical interference with other organs and the possibility of rupture.

Aspiration has been found dangerous and futile. It should not be thought of for diagnostic purposes. Moynihan stated that it should be considered only when the patient is ill from another disease and is suffering so acutely from pressure that the tension must be relieved in order to prepare the patient for laparotomy. In one case in our series scars of repeated aspirations, done elsewhere than at our clinic, were noted below the umbilicus.

Diabetes mellitus was present in three of the cases in our series. In one case the urine contained 1.33 Gm. of sugar per hundred cubic centimeters at the time of operation, but the urine was free from sugar a year later.

Persistent discharge from the fistula made by drainage may become a troublesome complication. Kerr [31] reported a case in which the fistula had drained for fifteen years. From 500 to 600 cc. of secretion was discharged daily from a fistula in a case of pancreatic cyst reported by Cushing.[32] Culler [33] treated two patients with roentgen rays to hasten closure. Hamilton [34] used radium in a fistula of a pancreatic cyst. Gutiérrez [35] transplanted a fistulous tract from the pancreas into the stomach. The wound healed rapidly and the patient recoverd. After marsupialization in our series the discharge persisted a few weeks, sometimes a few months, following which the patient did not complain further of symptoms referable to the cyst. In one case the cyst was drained twice. In a few instances, the wound continued to dis-

29. Willis, A. M., and Budd, S. W.: Pancreatic Cysts with Report of a Case, Surg. Gynec. Obst. **20**:688 (June) 1915.

30. Kosiński, J.: Annotations: The Pancreatic Juice in the Human Subject, Lancet **1**:948 (April 25) 1891.

31. Kerr, A. A.: Cysts and Pseudocysts of the Pancreas, with Report of Cases, Surg. Gynec. Obst. **27**:40 (July) 1918.

32. Cushing, H. W.: Traumatic Rupture of the Pancreas: Formation of Hemorrhagic Cyst; Operation, Followed by Pancreatic Fistula and Recovery, Boston M. & S. J. **138**:429 (May 5) 1898.

33. Culler, R. M.: Cure of Pancreatic Fistula by the Roentgen Ray, J. A. M. A. **75**:20 (July 3) 1920.

34. Hamilton, C. S.: Prolonged and Profuse Postoperative Drainage of Pancreatic Cyst and Use of Radium, Surg. Gynec. Obst. **35**:655 (Nov.) 1922.

35. Gutiérrez, A.: Implantation into the Stomach of a Pancreatic Fistula Following Cyst, Internat. Abstract Surg. **43**:214 (Sept.) 1926.

charge for as long as a year, and rarely for as long as two years. Boric acid ointment, collodion, or other protective substance has been spread over the skin about the wound. If the wall does not contain an epithelial lining, the cyst fills in gradually with granulation tissue. In our series, no patients returned to the clinic with sinuses that had drained for more than two years.

SUMMARY

A clinical analysis is presented of forty-seven cases of cyst of the pancreas in which operation was done at the Mayo Clinic in the past ten years. The tumor was felt above the umbilicus in more than 95 per cent of cases. Cholecystic disease was present in more than 34 per cent. More than 85 per cent of the patients in whom only cyst of the pancreas was found complained of pain. Nine of eleven cysts noted as being mobile were found to originate in the tail of the gland. With careful selection of cases for extirpation there was little difference as to risk and ultimate result between extirpation of the cyst and drainage.

UNDESCENDED TESTIS

PRINCIPLES AND METHODS OF TREATMENT *

HUGH CABOT, M.D.
AND
REED M. NESBIT, M.D.
ANN ARBOR, MICH.

Undescended testis is a condition frequently seen by the surgeon, especially the genito-urinary surgeon. As the condition is generally noted early in life by anxious parents, the patients are soon brought for expert opinion and advice, a fortunate occurrence, as practically all such afflicted children are thus seen by the medical profession early enough to escape permanent testicular damage incident on long delay in surgical correction.

Observers have differed regarding the incidence of this condition. Marshall [1] of Edinburgh, on examining recruits for the British and conscripts for the French armies, reported in 1828 an incidence of 1.02 per cent among 10,800 men examined. Zeibert,[2] 1898, reported an incidence of 0.2 per cent in 6,962,543 examined in the Austrian army between 1870 and 1882. Bevan [3] estimated the incidence at 1 in 500. The United States War Department [4] reported 3.1 per thousand men examined for the draft, or an incidence of 0.31 per cent.

It has been a constant observation that cryptorchidism occurs most frequently on the right side. In Coley's [5] group of cases, 238 were right-sided, 188 left-sided and 55 bilateral. Berger,[6] reporting 116 cases, found one-half to be right-sided, one-fourth left-sided and one-

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* From the Department of Surgery, University of Michigan Medical School.

1. Marshall, H.: Hernia Among Recruits for the British and Conscripts for the French Armies, Edinburgh, 1828.

2. Zeibert, K. A.: Ueber Kryptorchismus und seine Behandlung, Diss., Heidelberg, 1898.

3. Bevan, Arthur Dean: Operation for Undescended Testicle and Congenital Inguinal Hernia, J. A. M. A. **33**:773 (Sept. 23) 1899; The Surgical Treatment of Undescended Testicle, ibid. **41**:718 (Sept. 19) 1903; in Keen: Surgery, Philadelphia, W. B. Saunders Company, 1908, vol. 4, p. 592; Arch. f. klin. Chir. **72**:1035, 1904; Tr. Am. Surg. A. **47**:314, 1929.

4. Defects Found in Drafted Men, Draft Record, War Department, U. S. A., 1920.

5. Coley, W. B.: Operative Treatment of Undescended Testis with Reference to End-Results, Surg. Gynec. Obst. **28**:452, 1919.

6. Berger, P.: L'ectopie testiculaire de l'adulte, Rev. gén. de clin. et de thérap. **22**:12, 1908.

fourth bilateral. In our group, the left side was found to be most often afflicted.

The etiology of undescended testis is by no means a closed chapter. Many theories to explain this condition have been advanced. Some of them are as follows:

1. According to one theory, undescended testis is caused by conditions associated with the gubernaculum testis, such as paralysis of its muscle fibers, faulty attachment to the testis or even absence of gubernaculum.

2. Another theory is that the abnormality is caused by obstruction to the normal descent in the inguinal canal by either narrowing of the entire canal or stenosis of the external ring. This theory suffers badly when one considers that in many cases of cryptorchidism the testis can be drawn up into the inguinal canal readily by the mere force of the cremasteric reflex.

3. Another theory, interesting but difficult to believe, is that adhesions occur between the peritoneum and the testis, epididymis or spermatic cord. Some even go so far as to ascribe these adhesions to fetal peritonitis.

4. The length of the spermatic vessels has been given consideration by some as a cause. Observers have constantly noted shortness of the vessels and many have laid the blame there, but it has been suggested that this shortness is a result rather than a cause.

5. Turner[7] of Guy's hospital, in 1925, propounded a theory that faulty position of the fetus in utero causes abnormal pressure of the thigh against the inguinal canal and prevents complete descent of the testis into the scrotum.

Others have suggested that abnormalities of the testis or of the epididymis are responsible. The hereditary factor has also come in for its share of blame.

That any single cause is a constant etiologic factor is difficult to believe. Certain it is, however, that in operations for this deformity the shortness of the spermatic vessels offers the greatest obstacle to placing the testis in the bottom of the scrotum.

The undescended testis is generally found to be somewhat smaller and of softer consistency than normal. Accompanying indirect inguinal hernia of some degree is the rule, though this is not true in all cases. As previously mentioned, the spermatic vessels are always short and generally bound down by fascial bands and adhesions, their length determining the level at which the testis lies. The vas, on the other hand, is found to be of normal and adequate length, and in arrested

7. Turner, P.: Analysis of Results in Fifty Cases of Transseptal Orchidopexy for Imperfectly Descended Testicle, Guy's Hosp. Rep. **75**:209, 1925.

testes sometimes loops down out of the external ring into the scrotum. We have observed several such cases. The scrotum, while it varies considerably in size, often gives the appearance of being rudimentary. This appearance has led some observers to believe that failure of scrotal development plays an etiologic rôle. Observation of operative cases leads one to a contrary opinion.

All undescended testes eventually undergo morphologic and functional change. Hunter,[8] in 1791, pointed out that the abdominally retained testis was probably more defective than those arrested along the inguinal canal. Recent investigations by numerous observers, most notably Crew,[9] Fukui [10] and Moore,[11] have amply borne out this early observation. The work of Moore of Chicago is of more than passing interest in this connection. During the past ten years this investigator has done a tremendous amount of research work on animals of all types, and has definitely established the fact that elevation of temperature is the essential factor in retarded testicular development in cryptorchidism. Some of his experiments will bear citing. On progressively shortening the scrota of sheep and goats until the testes eventually lay flush against the body, progressive degenerative changes in the testes were noted so far as spermatogenesis was concerned. Likewise, experimental cryptorchidism, of both the abdominal and inguinal types, brought about these changes. He further established his thesis by ingeniously insulating the scrotum against loss of heat by radiation, and here again produced the same changes. On returning the testes to their normal scrotal position in the operative cases, and on deinsulating the others, he was able further to observe a return to normal spermatogenesis. Confirmatory evidence was also obtained by direct application of heat to the laboratory animals' genitalia for varying periods of time.

The morphologic changes within the undescended testis have been observed repeatedly, and observers are in agreement as to these changes. Briefly summarized, the accepted views are as follows:

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8. Hunter, John: Observations on Certain Parts of the Animal Economy, ed. 2, London, 1792, p. 1.

9. Crew, F. A. E.: A Suggestion as to the Cause of the Aspermatic Condition of the Imperfectly Descended Testis, J. Anat. **56**:98, 1921-1922.

10. Fukui, A.: On a Hitherto Unknown Action of Heat Ray on Testicles, Japan M. World **3**:27, 1923.

11. Moore, Carl R.: Cryptorchidism Artifically Produced, Proc. Am. Soc. Zool., Anat. Rec. **24**:383, 1922-1923; On the Relationship of the Germinal Epithelium to the Position of the Testis, ibid. **25**:142, 1923; The Behavior of the Testis in Transplantation, Experimental Cryptorchidism, Vasectomy, Scrotal Insulation and Heat Application, Endocrinology **8**:493, 1924. Moore and Chase: Heat Applications and Testicular Degeneration, Anat. Rec. **26**:344, 1923. Moore and Oslund: Experimental Studies on Sheep Testis, Anat. Rec. **26**:243, 1923. Moore and Quick: The Scrotum as a Temperature Regulator for the Testis, Am. J. Physiol. **68**:70, 1924.

1. The further the preadolescent testis has descended in its normal route, the more normal does it appear histologically.

Cooper,[12] in a gland at the external inguinal ring in an adult male, found parts showing complete spermatogenesis. Hobday[13] found spermatogenesis in testes that remained in the lower part of the inguinal canal, but in those found in the upper part of the canal or abdomen this was rare. Bland-Sutton[14] found, however, one case showing complete spermatogenesis in an abdominal testis.

2. The younger the age at which a retained gland is examined, the more nearly normal are its morphologic appearances.

Rawlings[15] found that undescended testes in boys under the age of 10 years show no morphologic changes, but in those examined after puberty it could readily be seen that the organ had not undergone changes incident to puberty.

Odiorne and Simmons[16] stated "testes though undescended are of normal structure during childhood but undergo none of the normal changes of puberty."

Cooper[12] found that cell differentiation and spermatogenesis began to develop at about the age of 11, and that at puberty the tubular cells began to show degenerative changes in the retained testis. Complete degeneration he found to be a slow process.

Bland-Sutton[14] suggested that retained testes may show spermatogenesis for a time after puberty.

Beigel[17] found active spermatozoa in the semen of a man, aged 22, with bilateral inguinal retention.

Odoirne and Simmonds[16] demonstrated active spermatogenesis in an undescended testis of a man, aged 30.

3. The interstitial cells of Leydig are apparently not influenced by the abnormal situation of a retained testis. As a matter of fact, some observers have noted an overabundance of this type of cell in the undescended testis (Cooper[12]).

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12. Cooper, E. R. A.: The History of the More Important Human Endocrine Organs at Various Ages, New York, Oxford University Press, 1925; Histology of the Retained Testis in Human Subjects at Different Ages and Its Comparison with Scrotal Testis, J. Anat. **64**:5, 1929.

13. Hobday, F. T. G.: Castration and Ovariotomy, ed. 2, London, W. & A. K. Johnston, 1914.

14. Bland-Sutton, J.: The Value of the Undescended Testis, Practitioner **84**:19, 1910.

15. Rawlings, L. B.: The Surgical Treatment of the Incompletely Descended Testis, Practitioner **81**:250, 1908.

16. Odiorne, W. B., and Simmons, C. C.: Undescended Testicle, Ann. Surg. **40**:962, 1904.

17. Beigel: Virchows Arch. f. path. Anat. **38**:144, 1867.

From these established facts, one can safely say: first, that orchidopexy had probably best be performed before the age of 9; second, that even after puberty and including the third decade, the operation may save a gland capable of some spermatogenesis, and third, that on account of active interstitial cell development in these glands, orchidectomy should never be given consideration at any age.

The incidence of malignancy has been given wide study, with investigators coming to no complete agreement. The preponderance of evidence would seem to indicate a greater incidence in the abnormally placed group. Surely the normally placed gland, by reason of its accessibility, will give evidence of abnormality earlier in event of malignant change than the abnormally placed one. We have felt that this alone should offer sufficient reason for performing orchidopexy at any age.

The earliest recorded orchidopexy was described by Rosenmerkel,[18] in 1820. This operation consisted merely of fixation of the testis to the fundus of the scrotum with a suture. Since that day about thirty different methods have been devised. Of these, a few bear mention as showing some variation in principle of procedure.

(1) Fixation of the testis to the fundus of the scrotum by various means, with further feature of a purse-string at the scrotal neck.

(2) Various types of traction by thread, wire or elastic stretched between the testis and the thigh, perineum, heel or wire frame.[19]

(3) By fixation to the thigh, such as in the Torek method.[20]

(4) By transplantation within the scrotum into the opposite scrotal sac, as in the Ombredonne operation.[21]

The first type has the objectionable feature of the purse-string above the testis, which may interfere with the circulation of the testis. The Bevan[3] operation, which falls in this group, has the further objectionable feature of dividing the spermatic vessels in those instances in which complete descent is otherwise impossible. Bevan excused this procedure by stating that the deferential artery that accompanies the vas is sufficient to supply the testis. Experience has hardly borne out

18. Rosenmerkel: Ueber die Radicalcur des in der Weiche liegenden Testikels bei nicht vollendeten Descensus desselben, Munich, J. Lindauer, 1820.

19. Bidwell, L. A.: A Modified Operation for the Relief of Undescended Testis, Lancet **1**:1439, 1893. Lanz: Der ektopisch Testikel, Zentralbl. f. Chir. **16**:425, 1905. Delbet, P.: De l'ectopie testiculaire et de son traitement par la fixation cutanée prépubienne du testicule, Assoc. franç. de chir. **19**:754, 1906.

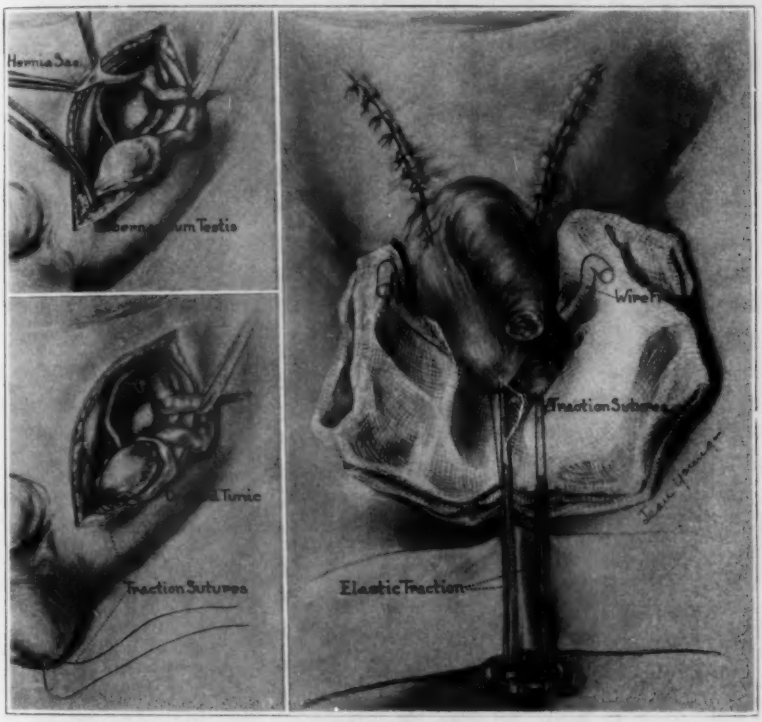
20. Torek, F.: New York M. J. **90**:948, 1909. Meyer, H. W.: Undescended Testicle, Surg. Gynec. Obst. **44**:53, 1927.

21. Ombredonne, L.: L'orchidopexie chez l'enfant, Gaz. méd. de France **2**:118. 1928. Higgins and Welti: Surgical Treatment of Undescended Testis, Surg. Gynec. Obst. **48**:536, 1929.

this assertion.[22] The Torek method of fixation to the thigh as well as the transscrotal orchidopexy offer the objection that they are formidable procedures and applicable only in cases in which complete descent of the testis can be obtained.

TECHNIC

During the past two years at the University Hospital clinic, a method utilizing the principle of constant traction has been employed. A skin incision is made from 2 to 3 inches (5 to 7.6 cm.) in length, extending from the internal inguinal



Operative procedure.

ring down to the neck of the scrotum. The inguinal canal is opened in the usual manner, the external ring being incised. The testis and cord are then exposed and isolated. The processus vaginalis is next dissected carefully from the cord structures and dealt with as any indirect inguinal hernial sac. When a complete hernial sac is found, we think it unwise to close the lower end of the processus vaginalis as hydrocele is almost certain to follow. The cord structures are now freed up to the internal ring from the many fibrous bands that are found to be surrounding them and producing much of their apparent shortening. With one finger in the retroperitoneal space, the spermatic vessels are freed from the posterior surface of the peritoneum. The cord structures will now be found to permit a fairly normal descent of the testis. A finger is next pushed down into

22. Mixter: Undescended Testicle in Children, Boston M. & S. J. **75**:63, 1916.

the scrotum to establish a bed in which the testis is to lie. A long catgut suture with a straight needle at each end is then passed through the remains of the gubernaculum at its lowest point and tied so that the two ends can be used for traction on the testis. The needles are then introduced into the scrotum and pushed out through the skin at the lowest point, about 0.5 cm. apart. With the sutures so placed, the testis is drawn well down into the scrotum. The sutures are then attached to a wire frame and rubber band so as to produce constant gentle downward traction on the testis. The inguinal incisions are next closed by any method that will give greatest length to the cord. The traction thus applied is left on for about twelve days, being adjusted occasionally during that period so as to remain constant. It has been found in many cases in which the testis can only be brought down to just outside the external ring at operation, that after a few days of such elastic traction the testis descends well down into the scrotum.

RESULTS

The principle involved in this technic is simple, the obtaining of permanent lengthening of vessels by continuous stretching. Our observations have seemed to prove this point satisfactorily.

In this regard, one case of our series is of particular interest. In a patient 9 years of age in whom the left testis was found to lie at the internal ring, it was brought down by dissection and subsequent traction to just outside the external ring. Eight months later he was reoperated on. On this occasion it was possible to bring the testis down to the midscrotal region, and twelve days after operation, when the traction was removed, the testis was in its normal scrotal position, and has so remained after twelve months.

We feel that this simple two-stage operation is definitely indicated in those cases in which complete reposition cannot otherwise be obtained without cutting the spermatic vessels.

In our series of twenty-five cases here reported, covering a two-year period, six were found to be bilateral, thirteen left-sided and six right-sided. The youngest person operated on was 3 years of age, the oldest 19.

Of the cases here reported we have been able to secure recent data on seventeen. Among these, the testis is in the normal scrotal position in ten instances, and in the upper part of the scrotum in seven; in none was it at a higher level. In thirteen, the testes are reported as being of normal size, two slightly larger than normal, one slightly smaller than normal and one definitely atrophic.

As this procedure has been used for only two and one-half years, one cannot, of course, give end-results. That will take time. Our post-operative results have thus far been satisfactory, and we recommend this procedure as safe, simple and apparently physiologic.

FORTY-FOURTH REPORT OF PROGRESS IN ORTHOPEDIC SURGERY*

PHILIP D. WILSON, M.D.

LLOYD T. BROWN, M.D.

M. N. SMITH-PETERSEN, M.D.

AND

JOHN G. KUHNS, M.D.

BOSTON

RALPH K. GHORMLEY, M.D.

ROCHESTER, MINN.

MURRAY S. DANFORTH, M.D.

PROVIDENCE, R. I.

GEORGE PERKINS

LONDON, ENGLAND

ARTHUR VAN DESSEL, M.D.

LOUVAIN, BELGIUM

AND

C. HERMANN BUCHOLZ, M.D.

HALLE, GERMANY

CONGENITAL DEFORMITIES

Congenital Torticollis.—Using the sartorius muscles of the dog, Middleton [1] repeated and confirmed Brook's experiments on the effects of ligation of artery and of vein, together and separately, in respect to the production of ischemic necrosis. The results of these experiments led Middleton to believe that congenital torticollis was due to an ischemic contracture resulting from obstruction (during prolonged childbirth) to the venous return from the sternal head of the sternocleidomastoid muscle. His paper contained a colored photomicrograph of a section from a tumor of the sternocleidomastoid muscle in a child, 4½ months of age, which is almost identical with a section from the sartorius muscle in a dog eight weeks after ligation of the vein only.

[ED. NOTE.—The causation of congenital torticollis has never been satisfactorily explained. Middleton's studies throw new light on the

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*This Report of Progress is based on a review of 266 articles selected from 486 titles dealing with orthopedic surgery appearing in the medical literature between Sept. 15, 1930, and Jan. 1, 1931. Only those papers which seem to represent progress have been selected for review.

1. Middleton, D. S.: Brit. J. Surg. **18**:188 (Oct.) 1930.

subject, and point strongly to ischemic contracture as the etiologic factor. We hope that this work will be confirmed by additional investigation.]

Spina Bifida Occulta.—Jelsma and Spurling [2] lamented the fact that relatively little had been written concerning spina bifida occulta. For this reason the true incidence of the condition was not known. It seemed fair to assume, however, that it was not uncommon, though many patients with this anomaly did not present symptoms. The clinical observations were divided into three main groups: the local signs, the neurologic manifestations and other anatomic anomalies. Operative treatment was the only method of cure, and this consisted in relieving pressure by the removal of a fibrolipomatous mass or by division of a fibrous membrane spanning the defect.

[ED. NOTE.—The point to be emphasized is that although spina bifida occulta is a common roentgenologic observation, it rarely gives rise to symptoms.]

Congenital Pseudarthrosis of the Tibia.—Camurati [3] defined congenital pseudarthrosis of the tibia as a localized dystrophy of the bone which might be associated with a similar lesion of the fibula. The total number of cases found by him in the literature was 118. At the Rizzoli Institute there were 27 cases in thirty-two years, or 0.98 per cent of the number showing congenital dislocation of the hip. There was a slight predominance of males in the series (57.62 per cent). The condition was rarely bilateral. Heredity did not play a part. A familial tendency was rare. Other congenital anomalies occurred in 11.03 per cent. Camurati believed that the condition was due to some embryonal change. He felt that glandular secretions (hypofunction and hyperfunction) and toxins might also play a considerable part in producing the change. The visible characteristic signs were deviation of the axis of the limb, atrophy of the leg, scar formation and vasomotor changes. A change in the size of the bone and, in some instances, abnormal mobility could be felt. The hip and knee were normal in their movements; the foot was limited in dorsal flexion.

The roentgenologic characteristics varied. In one type there was a curvature of the bone with atrophy of the diaphysis but thickening of the cortex at the site of the apex of the curvature, so that the medullary canal was lessened or obstructed. In the second type there was interruption of the continuity of the bone. In the third and most serious type there were marked changes in the ends of the bone at the site of the interruption, the ends being pointed and sometimes widely separated. Microscopic studies had rarely been made, and had yielded little definite information.

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2. Jelsma, F., and Spurling, R. G.: Surg. Gynec. Obst. **51**:537, 1930.
3. Camurati, M.: Chir. d. org. di movimento **15**:1 (July) 1930.

The treatment in the second and third types, differentiated by roentgenograms, was either a massive bone graft or, in the second type, an osteoperiosteal graft. Immobilization of the bony surfaces in strict contact was essential. The prognosis was uncertain, but in one group (not the author's) of 97 cases cure was obtained in 30 cases, 6 of which were of the most grave type. Of the cases studied by the author improvement was obtained in 16, or 23.8 per cent, while in 51 cases no improvement was noted.

GROWTH DISTURBANCES OF BONE

Marble Bones.—Pirie [4] reported 5 additional cases of marble bones (Albers-Schönberg's disease). Four of these cases occurred in one family, the mother and three children. The author found that the earliest roentgenologic sign of this disease was a dense band at the end of the diaphyses. This was most commonly seen at the lower end of the femur and at the upper end of the tibia. A little later a certain amount of clubbing was seen at the ends of the long bones. The dense shadows extended more and more into the epiphyses and into the shaft of the bone. In the older cases dense shadows were seen in the carpal bones, most frequently the scaphoid. These dense shadows were distributed irregularly through the skeleton. If the disease was widespread throughout the skeleton, a certain amount of anemia occurred, owing to encroachment on the medullary cavity. Postmortem examination of such bones showed that the hardness was like that of chalk rather than that of marble. Microscopically the diaphyses showed calcified cartilage with irregular myeloid spaces. There were numerous small areas of ossification. No abnormality in the blood calcium or phosphorus was found. No fractures had occurred in these children. The author suggested a widespread infection as the cause of the disease.

Osteochondritis Juvenalis.—Harbin and Zollinger [5] discussed the various disturbances of growth centers known as osteochondritis, including the conditions known as Legg-Calvé-Perthes' disease, Osgood-Schlatter's disease, Köhler's disease, etc. They pointed out that osteochondritis involved either the primary or the secondary centers of ossification, and the various conditions were classified accordingly. The disease was self-limited, and usually healed spontaneously with or without deformity. It was felt that cases of coxa plana might in later years give rise to mechanical or traumatic arthritis. To obtain physiologic rest during the acute state, immobilization was advised for as long as from four to six weeks. When it was possible to dispense with plaster, some other form of apparatus might be used to prevent

4. Pirie, A. H.: Am. J. Roentgenol. **24**:147, 1930.

5. Harbin, M., and Zollinger, R.: Surg. Gynec. Obst. **51**:145, 1930.

deformity until the active growth of the ossification center was completed. It was stated that while the cause of the condition was unknown, direct or indirect trauma usually played an important part.

[ED. NOTE.—We question whether it is often necessary to employ immobilization even in the acute stage of this condition. The disease is frequently symptomless, and we do not believe that any evidence has been adduced to show that its course can be modified by treatment.]

CALCIUM METABOLISM AND METABOLIC DISTURBANCES OF BONE

Calcium Requirements of the Body.—In an editorial [6] appearing in the *Journal of the American Medical Association* it was stated that calcium constituted about 1.5 per cent of the body—amounting to nearly 3 pounds (1.3 Kg.) in the adult male. Of this, over 99 per cent was present in the bones. The bones provided a ready source of calcium which had a far greater "mobility" or freedom of liberation and transport than was generally suspected. The best estimates currently available suggested the advisability of a daily intake of 1 Gm. or more of calcium in order to prevent loss of the indispensable element. Calcium was unevenly distributed in human foods; most food contained very little calcium. The cereal grains, tubers, meats, fish and fruits, all of which are prominent in the dietary of omniverous man, were comparatively poor in calcium.

Vitamin D as a "calcium-mobilizing" factor was not a substitute for calcium. At birth the body had a low calcium content, and its normal development involved a large increase, not only in the amount, but also in the percentage that it contained, and so required a liberal supply of calcium in the food.

Milk was the best natural source of calcium. Recent investigations had proved that calcium was advantageously absorbed from most foods other than milk and also from artificial inorganic supplements of calcium to the diet. Healthy women who had ingested alternately milk and calcium lactate under otherwise comparable dietary conditions appeared to utilize the inorganic calcium as effectively as the calcium of the raw milk.

Calcium Metabolism in the Healing of Fractures.—Bellelli [7] studied the calcium and phosphorus content of the blood in 14 persons with fractures. He concluded that a study of the calcium curve was of some value in the convalescence from fractures. He found that the blood calcium diminished in 90 per cent of the cases during the first few days to between 2 and 2.5 mg. per hundred cubic centimeters of blood.

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6. In Praise of Calcium, editorial. J. A. M. A. **95**:1977 (Dec. 27) 1930.
7. Bellelli, F.: Riforma med. **46**:966, 1930.

The calcium and phosphorus rose to values above the normal on the eighth or ninth day in young patients and on the seventeenth to the twentieth day in adults.

Lewis [8] studied 17 cases of fracture of the shaft of the long bones to determine whether the administration of viosterol had any effect on hastening union or callus formation. The amount of calcium and inorganic phosphorus of the blood was not materially raised; an average of 0.4 mg. for the calcium and practically no change for the phosphorus were obtained. He concluded that the use of viosterol did not hasten union or callus formation in adults.

Administration of Vitamin D and of Phosphorus.—Holmes and Pigott [9] tested the antirachitic activity of six samples each of five brands of viosterol 100 D in comparison with samples of ergosterol without D and ordinary cod liver oil. It was found that the healing effect of the various samples of viosterol was far from standard, and that some specimens possessed much greater potency than others. This fact makes it difficult for the practitioner to estimate the proper dosage. They suggested that the use of cod liver oil, although necessitating larger doses, might be more satisfactory, for while viosterol has only an antirachitic factor, cod liver oil has this factor and is rich in vitamin A as well.

Compere [10] studied the effect of phosphorus in 11 cases of severe rickets during the winter months. He found that while phosphorus given alone in doses of 1/100 grain (0.6 mg.) twice daily had practically no effect on the rickets, its addition to cod liver oil hastened the healing of the rickets. The use of both cod liver oil and phosphorus cleared up the rickets more quickly than cod liver oil alone.

Influence of Parathyroid Gland.—Speed and Rider [11] produced fracture in four dogs on which a thyroparathyroidectomy had been performed previously. Tetany was controlled by giving calcium lactate and thyroid extract. The low blood calcium and the imperfect and irregular healing of the fractures suggested to the authors that the calcium was directed away from the bones after parathyroidectomy.

Jaffe and Bodansky [12] produced changes in the long bones of growing puppies similar to those found in osteitis fibrosa cystica by injecting parathyroid extract (parathyroid extract-Collip) over long periods of

8. Lewis, K. M.: Ann. Surg. **92**:415, 1930.

9. Holmes, A. D., and Pigott, M. G.: New England J. Med. **203**:220, 1930.

10. Compere, E. L.: Effect of Phosphorus in Rickets, Am. J. Dis. Child. **40**: 941 (Nov.) 1930.

11. Speed, K., and Rider, D. L.: Experimental Healing of Bone After Parathyroidectomy, Arch. Surg. **21**:679 (Oct.) 1930.

12. Jaffe, H. L., and Bodansky, A.: J. Exper. Med. **52**:669, 1930.

time. They believed that the changes produced were similar to those found in some patients with hyperparathyroidism, i. e., a negative mineral balance and decalcification of the skeleton.

NEOPLASMS

Cysts in the Long Bones of the Hands and Feet.—Platt [13] reported a series of 20 cases of cysts of the long bones of the hand and the foot. The bones involved, in order of frequency, were the proximal phalanges, the metacarpals and, rarely, the metatarsals. The cysts originated in the metaphysis. The digit most commonly affected was the fifth finger. The majority of the growths remained latent until discovered roentgenologically after local injury. Incomplete spontaneous fracture occurred in half the patients. Microscopic examination showed chondroma in 8 cases and osteitis fibrosa in 5 cases. The author stressed the rarity of other types of bone tumors in the hands and feet, although in his paper he recorded an example of a giant cell tumor affecting the first metacarpal. The differential diagnosis between chondroma and osteitis fibrosa could not be made on clinical or roentgenographic evidence, although it frequently was possible at operation; the myxochondroma exhibited a cavity filled with white, glistening, friable, granulating tissue and soft cancellous bone, and without any definite lining; the osteitis fibrosa cyst revealed a cavity that was empty or incompletely filled with fibrous tissue and that had a tough fibrous lining which peeled easily.

Although spontaneous obliteration of an osteitis fibrosa cyst was known to occur frequently, Platt advocated operative intervention in all cases, owing to the difficulty of distinguishing between osteitis fibrosa and chondroma and the well known tendency of the latter tumor toward local malignancy. In a young patient in whom roentgenograms show the cyst to have a thick-walled cortical boundary it might be worth while to postpone operation pending roentgen evidence of expansion of the cyst.

The routine treatment at operation was to eradicate the contents by curettage, to cauterize the walls with pure phenol and to help obliterate the cavity by the insertion of an autogenous bone graft. The author reported no failures after this type of operation; in every case the cyst had disappeared and had been replaced by bone.

Articular Fibro-Endothelioma.—Wagner [14] reported 2 cases of a definitely encapsulated tumor arising from within a joint, one in a knee and the other in the anterior part of the ankle joint. These were diagnosed as fibro-endothelioma.

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13. Platt, H.: Brit. J. Surg. **18**:30, 1930.

14. Wagner, L. C.: Ann. Surg. **92**:421, 1930.

The diagnosis of this condition was difficult. There was swelling in only one part of the joint, and there was no particular tenderness or increase of synovial fluid. The range of motion was little affected, because the tumor was not in the articular or periarticular structures. Careful study of the roentgenograms with special attention to the structure of soft tissues was helpful. The treatment was surgical, and although a complete enucleation might be secured, the tumors were prone to recur. Roentgen treatment or Coley's toxin should be tried, but so far no cures had been reported. The tumors were removed as they recurred. Amputation of the affected extremity was usually necessary to effect a cure.

TUBERCULOSIS

Complement-Fixation Tests for Diagnosis.—Wadsworth, Mattoner and Stevens [15] performed complement-fixation tests for tuberculosis in 1,002 patients. Of 628 patients with pulmonary infection (supposedly tuberculosis) 546, or 86.9 per cent, reacted positively with at least one tubercle antigen. Of patients in whom acid-fast bacilli were recovered from the sputum 344, or 92.2 per cent, reacted positively. The serums in 40 cases of extrapulmonary tuberculosis were examined; 21, or 52.5 per cent, reacted positively. Of 314 patients with no clinical evidence of tuberculosis 44, or 14 per cent, gave a positive reaction. The author felt that the test was already of diagnostic value and that the reaction was proportional to the activity of the tuberculous process. The complement-fixation test in extrapulmonary tuberculosis gave too variable results to be of value.

Protective Vaccination.—Calmette [16] first vaccinated infants against tuberculosis in 1921. From that time until November, 1928, 116,180 infants had been so treated in France alone. He considered it a safe procedure. The duration of immunity was not accurately known, but the vaccination could be repeated without harm. In France the death rate for tuberculosis was 3.4 per cent for vaccinated, and 15.9 per cent for nonvaccinated infants.

Diagnostic Importance of Paravertebral Abscess.—The diagnostic importance of the paravertebral abscess of Pott's disease was discussed by Rigler, Ude and Hanson.[17] The differential diagnosis was also emphasized, the other important conditions to consider being osteomyelitis and mediastinal tumors. Various authors quoted by Rigler reported the presence of abscess in Pott's disease in from 20 to 66 per

15. Wadsworth, A. B.; Mattoner, E. J., and Stevens, B. S.: Am. Rev. Tuberc. **22**:539, 1930.

16. Calmette, A.: M. J. & Rec. **132**:119, 1930.

17. Rigler, L. G.; Ude, W. H., and Hanson, M. B.: Radiology **15**:471, 1930.

cent of the cases. Often the abscess was the earliest roentgen sign and might appear before there was evidence of destruction of bone. This was true in 2 cases reported by the authors.

Nonoperative Versus Operative Treatment.—Rollier [18] reported the results of his method of treatment, which was a combination of heliotherapy, orthopedics and rational diet. The orthopedic treatment included rigorous maintenance of the horizontal decubitus, although it did not involve complete immobilization of the affected point. The use of extension allowed of a cautious and gradual separation of the surface of the joint and avoided painful compressive ulceration. While maintaining relative immobility, it allowed small spontaneous movements of the joint which helped the deep circulation and hastened the healing of the foci in the bone and the regeneration of the cartilages. The fact that restoration of the cartilages occurred was, according to Rollier, clearly shown by the reappearance of the joint space in the roentgenograms, and it was this that explained the frequency with which movement and function were recovered.

Rollier reported the following end-results:

	Hip	Knee	Foot
Cure maintained with function, per cent	74.0	66.4	92.6
Cure maintained with normal function, per cent	33.6	41.9	67.0
Cure maintained with partial function, per cent	66.4	58.1	25.0
Ankylosis, per cent	26.0	33.6	7.2

Lo Grasso,[19] in discussing the nonoperative treatment of tuberculous joints of the lower extremity, stated that a patient with a tuberculous joint should be treated for the systemic infection and that the disease of the joint should be treated as a complication and not as the primary infection. He felt that operative procedures were likely to disseminate the disease if undertaken during the acute state. Surgical measures, if necessary, should be undertaken only after a preliminary course of conservative treatment in order to raise the resistance of the patient as much as possible. In his experience conservative treatment usually resulted in healing with useful motion of the joint and without recurrence of the disease.

Hibbs [20] reported on the operative fusion of tuberculous joints of the lower extremity. Fusion was obtained in all the joints operated on except in 11 cases of tuberculosis of the hip joint (8 per cent of 150 cases). There were 154 cases of tuberculosis of the hip joint, 18 cases of tuberculosis of the ankle joint and 4 cases of tuberculosis of

18. Rollier, A.: J. Bone & Joint Surg. **12**:733, 1930.
19. Lo Grasso, H.: J. Bone & Joint Surg. **12**:755, 1930.
20. Hibbs, R. A.: J. Bone & Joint Surg. **12**:749, 1930.

the tarsal joints in which the operation was performed during this period of study. There had been no recurrence of the disease in any of the fused joints. The activities of the patients had not been limited by the operation. Because of the compensatory motion in the lumbar spine the patients whose hips had been fused were free from almost any handicap. The author felt that a great advantage of the fusion operation was that it freed the patients from the danger of extension of the disease from the focus in the joint as well as from long, uncertain treatment in hospitals or clinics.

[ED. NOTE.—The divergence between the nonoperative attitude, as exemplified by Rollier and Lo Grasso, and the point of view favoring surgical intervention, as represented by Hibbs, seems as wide as ever. Rollier's article is of importance in that for almost the first time he reports remote results, the sole criterion that should be employed in judging the results of treatment. These results are impressive, and no one employing similar methods in this country has been able to duplicate them. On the other hand, Hibbs reports remarkably good results from fusion operations, and these results can be duplicated by good surgeons anywhere. Taking into consideration economic, social, climatic and geographic factors in the United States, operative treatment seems to offer more in bringing about a cure than nonoperative treatment. We agree with Lo Grasso, however, that the patient must also be treated systemically for the primary infection and to arrest further extension of the disease, and that preferably such treatment should precede rather than follow operation.]

POLIOMYELITIS

Immune Serum Reactions.—Aycock and Kramer [21] tested the blood serums of 12 mothers and their infants for neutralizing substances against the virus of poliomyelitis. Ten of the mothers with their newborn infants neutralized the virus, as shown by intracerebral injection into monkeys. In 2 cases the virus was not neutralized. The authors felt that these observations pointed to a passive transmission of immunity from mother to infant.

In a recent editorial [22] in the *Journal of the American Medical Association* the poliomyeliticidal action of normal human serum was discussed. The serum of persons who had recovered from poliomyelitis usually, though not invariably, had the power of killing, neutralizing or inactivating poliomyelitis virus in vitro. It was generally assumed, though

21. Aycock, W. L., and Kramer, S. D.: J. Exper. Med. **52**:457, 1930.

22. Poliomyeliticidal Action of Normal Human Serum, editorial. J. A. M. A. **95**:1269 (Oct. 25) 1930.

without experimental proof, that this neutralizing power was a measure of the probable therapeutic value of such serums. Relatively few control tests had been made with normal human serums, the general assumption being that while the serums might occasionally neutralize poliomyelitis virus in vitro, they were usually inert or of such low viricidal power as to be of little or no therapeutic interest. Shaughnessey, Harmon and Bordon concluded from their investigation that serums from family contacts and normal children over 2 years of age possessed greater power to neutralize poliomyelitis virus than serums from persons who had recovered from an attack of the disease. Of even greater theoretical interest were the few tests made with serums from normal children under 2 years of age. Of the five serums from persons who had recovered from poliomyelitis thus far tested by the Chicago investigators none had neutralized virus in a dilution as high as 1 : 10. On the other hand, nearly 90 per cent neutralizations were obtained in 1 : 10 dilutions with the serums of normal children over 2 years of age. This observation suggested that in the normal infantile population immunization against poliomyelitis proceeded in much the same way as that against diphtheria.

PYOGENIC INFECTIONS

Reparative Process in Chronic Osteomyelitis.—A study of the healing process in chronic osteomyelitis was made by Kreuscher and Hueper.[23] In a series of 16 patients in whom the "saucerization operation" had been performed, tissue for study was obtained at varying intervals from the ulcerated region, including the epithelized border zone and superficial parts of the bone. In all cases evidence of a more or less advanced healing process was observed. In a few instances biopsies were performed repeatedly at intervals of from four to six weeks, beginning thirty days after the operation. The writers found that the bony defect was filled in by the production of three different zones of tissue formed in succession, namely, granulation tissue, strong fibrous and hyalinized connective tissue and loose connective tissue with lamellae of osteoid and osseous tissue. The presence of infection interfered to a greater or lesser extent with the proper formation and arrangement of these structures and therefore greatly retarded regeneration of bone. In the sections examined, no evidence of an attempt at formation of cortical bone was apparent. A loose, sometimes edematous connective tissue was present between the bony lamellae. In a single case there was an attempt at formation of cortical bone. In this instance complete epithelization of the defect had existed for six

23. Kreuscher, P. H., and Hueper, W. C.: J. Bone & Joint Surg. **12**:541, 1930.

months. The formation of cortex evidently occurred at a late period in bony regeneration. The same condition was found in regard to the formation of periosteum. Elastic tissue was only scantily present in the tissue covering the new-formed bone. The observations seemed to indicate that a prognostication of the postoperative healing process of chronic osteomyelitis from biopsy sections was possible, and that valuable information in regard to therapeutic management of the individual case might be obtained in this way.

ARTHRITIS

Classification, Causation and Treatment.—The unusual interest that has recently been aroused in the study of chronic polyarticular arthritis is shown by the publication of symposia dealing with all phases of the subject, as well as by a number of articles of merit scattered throughout the medical literature.

Osgood [24] divided arthritis into two types according to the nomenclature of the American Committee for the Control of Rheumatism: atrophic and hypertrophic. The committee agreed that at the present time no single infectious agent, completely defined dietary deficiency or metabolc disturbance had been conclusively shown to be the sole cause of arthritis. The committee inclined to the belief that any one of these factors or certain combinations of them under appropriate circumstances might basically underlie the onset of the disease.

Swaim [25] gave a résumé of seventeen years' experience in the treatment for arthritis. He found it helpful to divide the disease into infectious, atrophic and hypertrophic types. In the infectious type the removal of foci of infection and careful treatment with vaccines were efficacious after the general condition of the patient had been sufficiently improved. In the hypertrophic type the correction of the faulty body mechanics and the use of endocrine products as indicated offered most in treatment. He found a distinct hereditary tendency in the atrophic type. Here, no matter what the precipitating cause had been, the depleted physical condition, lack of resistance and metabolic instability were the factors that permitted the precipitating cause to become active. Early recognition and treatment of these underlying conditions would probably have prevented arthritis in a number of the patients.

Cecil [26] stated that the atrophic type of arthritis was, in the acute onset, secondary to a bacteremia. A preceding trauma to the joint or

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24. Osgood, R. B.: Orthopedic Aspects of Chronic Rheumatism or Arthritis, J. A. M. A. **95**:992 (Oct. 4) 1930.

25. Swaim, L. T.: J. Lab. & Clin. Med. **15**:1171, 1930.

26. Cecil, R. L.: J. Lab. & Clin. Med. **15**:1177, 1930.

a possible hypersensitiveness of the tissues was necessary for arthritis to develop. He was unable to determine the rôle played by allergy. In the hypertrophic type no definite evidence of infection had been found. The most probable causes were endarteritis of the small blood vessels and trauma in persons who were overweight and who showed senile changes in the tissues. Heredity seemed to play a definite rôle in hypertrophic arthritis. A review of the bacteriologic investigation in arthritis was given.

Fletcher [27] found that a liberal use of vitamins and a moderate restriction of carbohydrates were valuable measures in the treatment for arthritis, particularly when roentgenograms showed functional abnormalities in the enteric tract. After the feeding of vitamin B in large amounts, he noticed improvement in tone in the large bowel and a reappearance of the haustral markings. Large quantities of carbohydrate seem to favor the development of deficiency diseases.

Crowe,[28] reiterating his belief that all cases of arthritis were due primarily to bacterial infection, discussed his method of treatment with vaccine. This consisted in giving the smallest possible dose that stimulated the tissue cells. He believed that a local reaction should be avoided if possible, and that a general reaction should never be produced. The criterion of an effective dosage was a decrease in the swelling, pain and stiffness of the joints. Stock vaccines, including a number of varieties of nonhemolytic streptococci and *Micrococcus deformans,* were used as a rule, and had been found to be as effective in most cases as autogenous vaccines.

Ely [29] observed that the same pathologic lesions in the joint might be produced by many different conditions. Atrophic, or type 1, arthritis he believed to be due entirely to bacteria. In many patients with this variety of arthritis the lesions of the joints healed when the supply of bacteria was shut off by the removal of foci of infection; in others, the bacteria were capable of maintaining an indepedent existence in the joints. The cause of hypertrophic, or type 3, arthritis remained unknown. The disease might originate from the presence of living organisms, presumably protozoan, in the bone near the joint. These organisms were normally considered harmless when found in the intestinal tract. They might gain entrance at the root of a dead tooth. In such cases extraction of dead teeth and administration of parasiticides were indicated. In most cases of arthritis the ruthless removal of so-called foci of infection was unnecessary, unscientific and often harmful.

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27. Fletcher, A. A.: J. Lab. & Clin. Med. **15**:1140, 1930.
28. Crowe, H. W.: J. Lab. & Clin. Med. **15**:1072, 1930.
29. Ely, L. W.: J. Lab. & Clin. Med. **15**:1264, 1930.

Allergic Arthritis.—Freiburg and Dorst[30] found what they called the allergic type of joint in more than 30 per cent of 100 cases of arthritis. The clinical picture was that of a fusiform swelling with slight or no periarticular infiltration. There was moderate limitation of motion; the capsule of the joint was distended with fluid and "boggy" to palpation. Pain was usually slight. The patients sought treatment because of the stiffness or swelling. The fluid in the joint was clear and straw-colored, and contained a few cells, chiefly lymphocytes or large mononuclears. Cultures obtained from the fluid were negative. The physical properties of the fluid suggested a transudate rather than an exudate. Cultures were made of organisms obtained from the nose, sinuses, throat and enteric tract. Hypersensitiveness to these organisms was then tested by cutaneous reactions. A vaccine was made of the organisms giving positive cutaneous reactions. This vaccine was given in very small doses, the initial dose usually being 0.5 minim (0.03 Gm.).

Dietetics.—Snyder and Traeger[31] concluded from their clinical observations that proper dietary instruction was an important part of the therapy in arthritis. The patients were first placed on a basic diet, and this was regulated later in regard to the general condition, weight, clinical composition of the blood and clinical progress of the patient. This basic diet had the following characteristics: a low caloric value, a low carbohydrate value, an adequate vitamin content, elasticity and availability.

Results of Sympathetic Ganglionectomy.—Hench, Henderson, Rowntree and Adson[32] concluded from their observations of sympathetic ganglionectomy and trunk resection in 30 cases of chronic arthritis that these procedures had a limited application. As suitable for operation they selected patients with atrophic arthritis in whom the disease was chiefly periarticular, with little bony alteration except atrophy. Improvement after operation could be expected only in those cases in which definite peripheral vascular changes resulted when the sympathetic control was temporarily removed. This was tested by giving a large dose of typhoid vaccine. No patient was operated on who was over 45 years of age. In all the patients the disease was progressively getting worse but was mainly confined to the extremities. All of the patients were given general treatment for from six to twelve months before operation was considered. The effects of the operation were a marked vasodilatation, with an increased flow of blood in the capillaries, an

30. Freiburg, J. A., and Dorst, S. E.: J. Lab. & Clin. Med. **15**:1109, 1930.

31. Snyder, R. G., and Traeger, C. H.: J. Lab. & Clin. Med. **15**:1214, 1930.

32. Hench, P. S.; Henderson, M. S.; Rowntree, L. G., and Adson, A. W.: J. Lab. & Clin. Med. **15**:1247, 1930.

increased surface temperature in the extremities, the abolition of reflex sweating, loss of the pilomotor reflex, a positive Horner's syndrome and slight atrophy of the muscles of the shoulders. The relief from pain varied from complete relief to no change. The authors were unable to offer a satisfactory explanation for the relief from pain, and they felt that at the present time no definite statement could be made with regard to the value of these operative procedures in arthritis.

Gonorrheal Arthritis.—Kinsella [33] expressed the belief that allergy played a rôle in gonorrheal arthritis. The arthritis never appeared with acute urethritis, but usually followed an intercurrent infection or intoxication later. This suggested the development of a state of hypersensitiveness before symptoms appeared in the joints. The author recognized two types of gonorrheal arthritis: (1) a simple effusion into the joint, cured by aspiration and splinting, and (2) an extra-articular induration. For the second type incision and drainage of the most congested and tender areas were advised, followed by early motion in the joint.

Spinal Types of Arthritis.—In 80 unselected persons over 40 years of age, Cottrell [34] found ostearthritis of the spine by roentgenography in 44 per cent. The average age of the patients was 55.6 years, and the dorsolumbar region was the part most frequently involved. Thirty-one per cent showed evidence of pressure on the spinal nerve roots. In 17 cases (21 per cent) there were no arthritic symptoms. Eight patients (10 per cent) had the radicular syndrome, and of these, 5 had been operated on for supposed abdominal conditions without relief.

At a medicolegal conference, Putti [35] discussed the types of arthritis of the spine, classifying the two common types as spondylitis deformans and ankylosing spondylarthritis and calling attention to a third form of vertebral arthritis that involved the posterior articulations. The last type was shown infrequently and with difficulty by roentgenography. He believed that in cases of arthritis, trauma that seemed trivial might cause symptoms to develop in joints that had been "silent" previously, and that these symptoms might persist for long periods and disable the patients. Such arthritides were the cause of many disabilities in laborers. On the other hand, congenital anomalies rarely were important factors in causing persistent disabilities.

Sedimentation Tests.—Dawson, Sia and Boots [36] performed 500 sedimentation tests on 220 patients suffering from arthritis. They found

33. Kinsella, R. A.: J. Lab. & Clin. Med. **15**:1062, 1930.

34. Cottrell, J. C.: Surg. Gynec. Obst. **51**:731, 1930.

35. Putti, V.: Riforma med. **46**:999, 1930.

36. Dawson, M. H.; Sia, R. H. P., and Boots, R. H.: J. Lab. & Clin. Med. **15**:1065, 1930.

that the sedimentation rate was moderately or markedly increased in practically all cases of active atrophic arthritis. There was a fairly close relationship between the rate of sedimentation and the severity and extent of the arthritis. An increased sedimentation rate was commonly observed with exacerbations of the disease and a decreased rate with remissions. The sedimentation reaction tended to return to normal in cases that became arrested. In hypertrophic arthritis a slight increased sedimentation rate was usually found. Cases of myositis, fibrositis and neuritis showed the least variation from the normal (usually a very slight increase) in the sedimentation reaction.

Rheumatoid Nodules.—Dawson and Boots [37] studied the subcutaneous nodules found in rheumatoid (chronic infectious) arthritis. Bacteriologic investigations of these nodules gave entirely negative results. With the exception of those peculiar to rheumatic fever, similar nodules were not observed in any other disease. There was a striking resemblance between the subcutaneous nodules occurring in rheumatic fever and those observed in rheumatoid arthritis. This resemblance suggested the possibility that these two clinical entities might be different manifestations of the same fundamental pathologic process.

[ED. NOTE.—We are unable to draw any definite conclusions from these articles in respect to the causation of chronic arthritis. Evidently a number of factors play a part, even though microorganisms seem responsible for most of the actual changes in the joints. From the standpoint of treatment as much or more may be accomplished by efforts to render the soil less favorable than by attention directed only to the eradication of the seed. We regard it as distinctly encouraging and offering hope for the future that arthritis has come to occupy so prominent a position as a subject for study that such an excellent variety and quality of articles as those mentioned, dealing with various phases of the problem, should appear within a short period.]

VASCULAR DISTURBANCES OF THE EXTREMITIES

Smithwick and White [38] treated 11 patients with vascular disease of the lower extremity by injections of alcohol into the sensory nerves. This method permitted the painless dressing of gangrenous areas; infection could be more easily controlled and exercises could be done more easily to improve the circulation. It was felt that amputations were avoided by this means in 6 of the 11 cases. As a result of these alcoholic injections, sensation in the area supplied by the nerve was usually lost for from three to six months.

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37. Dawson, M. H., and Boots, R. H.: Subcutaneous Nodules in Rheumatoid (Chronic Infections) Arthritis, J. A. M. A. **95**:1894 (Dec. 20) 1930.

38. Smithwick, R. H., and White, J. C.: Surg. Gynec. Obst. **51**:394, 1930.

Morton and Scott [39] used spinal anesthesia, as employed in various operative procedures, to determine sympathetic vasoconstrictor activity in the lower extremities. In persons without vascular disease there was a fairly constant temperature for each part, showing a slightly varying but progressive rise in temperature (measured with a thermocouple) from knees to toes. After the injection of a spinal anesthetic the entire surface of the skin of the lower part of the leg attained approximately the same temperature. In vascular disabilities of a vasospastic nature the cutaneous surface of the lower part of the leg reached approximately the same temperature as in normal persons. When there was disease of the vessels or mechanical obstruction, no rise or only a slight rise was noticed after spinal anesthesia.

Posttraumatic Painful Osteoporosis.—Leriche and Fontaine [40] discussed the subject of painful posttraumatic osteoporosis. Following a peripheral traumatism, apparently not severe, there occurred stiffness, pain on use, atrophy and edema. Little importance was attached to these symptoms if the roentgenogram made after the accident showed the bones intact. Physical therapy was usually employed, often with aggravation of the situation. The symptoms became more severe, and after two or three months roentgenograms showed rarefaction of the epiphyses with the appearance of small cavities suggestive of tuberculosis. A plaster cast was applied; pain continued, and the cast was changed without improvement. After about six months the pain subsided, but the joint remained stiff. Finally, in ten or twelve months "healing" was complete, often with partial, but sometimes with total ankylosis.

This was the clinical picture of traumatic osteoporosis, but surprising transformations might result from sympathectomy. After sympathectomy (more often periarterial) one saw the rarefied bone reform both as to texture and outline and in a few weeks regain a normal roentgenologic appearance. Limitation of motion, pain and weakness disappeared. In a few hours the patient was better, and in a few days had the impression that he was cured. These facts were inexplicable. One might consider it as a law that active hyperemia created a rarefaction of bone, and that there was no rarefaction without hyperemia. It was paradoxical that sympathectomy which also produced hyperemia should have a beneficial therapeutic effect on this condition. The authors only presented the facts; the explanation was to be found later. It was probable that in conditions of hyperemia there were a variety of physiologic states that had not been completely differentiated. On the other hand, traumatic osteoporosis was not of purely vasomotor origin. The

39. Morton, J. J., and Scott, W. J. M.: J. Clin. Investigation **9**:235, 1930.
40. Leriche, R., and Fontaine, R.: Presse méd. **38**:617, 1930.

authors had treated 16 patients for this condition with periarterial sympathectomy. The pain had disappeared the same or the next day, and the patients had been able to effect movements which previously were impossible. The relief had been permanent.

[ED. NOTE.—This observation is important for three reasons; (1) The aforementionad paradox was noted; (2) an effective method of treatment seems to have been found; (3) a suitable name for a fairly frequent condition has been supplied. If rarefaction of bone results only from hyperemia, we should like to know how the authors explain atrophy of the bone following immobilization of an extremity.]

DISEASES OF THE NERVOUS SYSTEM

Sympathectomy in Spastic Paralysis.—In 1927, Royle on his visit to England performed ramisection on 6 patients selected by himself as likely to be benefited. These patients were seen prior to operation and were observed afterward by Symonds,[41] a neurologist, and by a group of six orthopedic surgeons whose conclusions in 1930 were: 1. The operation of cervical or lumbar ramisection is without effect on the rigidity due to extrapyramidal disease. 2. The rigidity of pyramidal disease, as seen in conditions of hemiplegia and quadriplegia in children, might be temporarily diminished after the operation. This temporary diminution of tone had been observed in both upper and lower limbs with some improvement of voluntary power. The diminution of tone and the improvement in function were, however, short-lived; within a few weeks or months, notwithstanding continuous measures of reeducation under experienced medical supervision, the condition of the patients remained as before the operation. In the opinion of several surgeons who examined these patients both before and shortly after the operation, the diminution of tone was no more than might be seen after any major surgical procedure with postoperative shock.

On the other hand, Wade[42] as a result of reviewing 38 cases concluded that the operation of ramisection with tenotomy and reeducation should be the procedure of choice in cases of spastic paralysis.

At the meeting of the British Medical Association at Winnipeg in 1930, Royle[43] reaffirmed his faith in his operation for the treatment for spastic paralysis, claiming that 70 per cent of his patients so treated had been benefited.

At the same meeting, Fulton[44] in discussing the mechanism of postural responses pointed out that the stretch reflex, which is at the

41. Symonds, C. P.: Lancet **2**:127 (July 19) 1930.
42. Wade, R. B.: J. Coll. Surgeons, Australasia **2**:406 (March) 1930.
43. Royle, N. D.: Lancet **2**:639 (Sept. 20) 1930.
44. Fulton, J. F.: Lancet **2**:645 (Sept. 20) 1930.

basis of posture, was abolished by division of either the posterior or the anterior roots but not by sympathectomy, although the transient diminution in rigidity occurring in spastic paralyses after ramisection suggested that the operation might cause an increase in the threshold for eliciting the stretch reflex. Fulton thought that apart from certain visceral conditions, such as Hirschsprung's disease, the only clearcut indication for sympathectomy was ischemia, and that any pathologic process in which healing would be greatly accelerated by an increased supply of blood offered an indication for ramisection.

(*To be continued*)

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